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=> s topoisomerse(a)II(a)poison

L1 0 TOPOISOMERSE(A) II(A) POISON

=> s topoisomerase(a)II(a)poison

L2 1540 TOPOISOMERASE(A) II(A) POISON

=> dis 13 1-21 bib abs

- L3 ANSWER 1 OF 21 MEDLINE on STN
- AN 2007557753 MEDLINE
- DN PubMed ID: 17622580
- TI A mouse model for studying the interaction of bisdioxopiperazines with topoisomerase IIalpha in vivo.
- AU Grauslund Morten; Thougaard Annemette Vinding; Fuchtbauer Annette; Hofland Kenneth Francis; Hjorth Peter Hansen; Jensen Peter B; Sehested Maxwell; Fuchtbauer Ernst-Martin; Jensen Lars H
- CS Experimental Pathology Unit, Department of Pathology, Rigshospitalet afs. 3731, Biocenter, Bygning 2, 3 sal., Ole Maaloes vej 5, DK-2100 Copenhagen O, Denmark.
- SO Molecular pharmacology, (2007 Oct) Vol. 72, No. 4, pp. 1003-14. Electronic Publication: 2007-07-10. Journal code: 0035623. ISSN: 0026-895X.
- CY United States

- DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
- LA English
- FS Priority Journals
- EM 200711
- ED Entered STN: 20 Sep 2007 Last Updated on STN: 8 Dec 2007 Entered Medline: 27 Nov 2007
- The bisdioxopiperazines such as (+)-(S)-4, 4'-propylenedi-2, 6-AΒ piperazinedione (dexrazoxane; ICRF-187), 1,2-bis(3,5dioxopiperazin-1-y1) ethane (ICRF-154), and 4,4'-(1,2-dimethyl-1,2ethanediyl)bis-2,6-piperazinedione (ICRF-193) are agents that inhibit eukaryotic topoisomerase II, whereas their ring-opened hydrolysis products are strong iron chelator. The clinically approved analog ICRF-187 is a pharmacological modulator of topoisomerase II poisons such as etoposide in preclinical animal models. ICRF-187 is also used to protect against anthracycline-induced cardiomyopathy and has recently been approved as an antidote for alleviating tissue damage and necrosis after accidental anthracycline extravasation. This dual modality of bisdioxopiperazines, including ICRF-187, raises the question of whether their pharmacological in vivo effects are mediated through interaction with topoisomerase II or via their intracellular iron chelating activity. In an attempt to distinguish between these possibilities, we here present a transgenic mouse model aimed at identifying the contribution of topoisomerase IIalpha to the effects of bisdioxopiperazines. A tyrosine 165 to serine mutation (Y165S) in topoisomerase IIalpha, demonstrated previously to render the human ortholog of this enzyme highly resistant toward bisdioxopiperazines, was introduced at the TOP2A locus in mouse embryonic stem cells by targeted homologous recombination. These cells were used for the generation of transgenic TOP2A(Y165S/+) mice, which were demonstrated to be resistant toward the general toxicity of both ICRF-187 and ICRF-193. Hematological measurements indicate that this is most likely caused by a decreased ability of these agents to induce myelosuppression in TOP2A(Y165S/+) mice, highlighting the role of topoisomerase IIalpha in this process. The biological and pharmacological implications of these findings are discussed, and areas for further investigations are proposed.
- L3 ANSWER 2 OF 21 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- AN 2008:312487 BIOSIS
- DN PREV200800316670
- ${\tt TI}$ A mouse model for studying the interaction of bisdioxopiperazines with topoisomerase ${\tt II}$ alpha in vivo.
- AU Grauslund, Morten; Thougaard, Annemette Vinding; Fuechtbauer, Annette; Hofland, Kenneth Francis; Hjorth, Peter Hansen; Jensen, Peter B.; Sehested, Maxwell; Fuechtbauer, Ernst-Martin; Jensen, Lars H. [Reprint Author]
- CS Rigshosp, Dept Pathol, Expt Pathol Unit, Bioctr, Bygning 2,3 Sal,Ole Maaloes Vej 5, DK-2100 Copenhagen O, Denmark lhj@topotarget.com
- SO Molecular Pharmacology, (OCT 2007) Vol. 72, No. 4, pp. 1003-1014. http://www.molpharm.org.
 CODEN: MOPMA3. ISSN: 0026-895X.
- DT Article
- LA English
- ED Entered STN: 21 May 2008 Last Updated on STN: 21 May 2008
- AB The bisdioxopiperazines such as (+)-(S)-4,4 '-propylenedi-2,6-piperazinedione (dexrazoxane; ICRF-187), 1,2-bis(3,5-dioxopiperazin1-yl) ethane (ICRF-154), and 4,4 '-(1,2-dimethyl-1,2-ethanediyl) bis-2,6-piperazinedione (ICRF-193) are agents that

inhibit eukaryotic topoisomerase II, whereas their ring-opened hydrolysis products are strong iron chelator. The clinically approved analog ICRF-187 is a pharmacological modulator of topoisomerase II poisons such as etoposide in preclinical animal models. ICRF- 187 is also used to protect against anthracyclineinduced cardiomyopathy and has recently been approved as an antidote for alleviating tissue damage and necrosis after accidental anthracycline extravasation. This dual modality of bisdioxopiperazines, including ICRF- 187, raises the question of whether their pharmacological in vivo effects are mediated through interaction with topoisomerase II or via their intracellular iron chelating activity. In an attempt to distinguish between these possibilities, we here present a transgenic mouse model aimed at identifying the contribution of topoisomerase II alpha to the effects of bisdioxopiperazines. A tyrosine 165 to serine mutation (Y165S) in topoisomerase II alpha, demonstrated previously to render the human ortholog of this enzyme highly resistant toward bisdioxopiperazines, was introduced at the TOP2A locus in mouse embryonic stem cells by targeted homologous recombination. These cells were used for the generation of transgenic TOP2A(Y165S/+) mice, which were demonstrated to be resistant toward the general toxicity of both ICRF-187 and ICRF-193. Hematological measurements indicate that this is most likely caused by a decreased ability of these agents to induce myelosuppression in TOP2A(Y165S/+) mice, highlighting the role of topoisomerase II alpha in this process. The biological and pharmacological implications of these findings are discussed, and areas for further investigations are proposed.

- L3 ANSWER 3 OF 21 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
- AN 2001:435706 BIOSIS
- DN PREV200100435706
- TI Topoisomerase II poison and bis-dioxopiperazine derivative combination therapy.
- AU Jensen, Peter Buhl [Inventor, Reprint author]; Sehested, Maxwell [Inventor]
- CS Farum, Denmark
 - ASSIGNEE: Topo Target ApS, Copenhagen, Denmark
- PI US 6265385 20010724
- SO Official Gazette of the United States Patent and Trademark Office Patents, (July 24, 2001) Vol. 1248, No. 4. e-file.

 CODEN: OGUPE7. ISSN: 0098-1133.
- DT Patent
- LA English
- ED Entered STN: 12 Sep 2001 Last Updated on STN: 22 Feb 2002
- AB The present invention relates to a method for selectively killing tumor or metastatic cells within a defined compartment of the organism of a large mammal, in particular a human, said method comprising administering to a mammal an effective tumor -- or metastasis-killing amount of a topoisomerase II poison except doxorubicin, and protecting non-tumorous tissue of the mammal against the toxic action of the topoisomerase II poison by administration of a bis-dioxypiperazine compound. In particular, the invention relates to a pharmaceutical kit for selectively killing tumor or metastatic cells within the central nervous system in a large mammal, in particular a human, said kit comprising: a) a dosage unit of a bis-dioxypiperazine and a pharmaceutically acceptable carrier, and b) a dosage unit of topoisomerase II poisons except doxorubicin and a pharmaceutically acceptable carrier.
- L3 ANSWER 4 OF 21 BABS COPYRIGHT 2008 BEILSTEIN MDL on STN
- AN 6710431 BABS

- TI A mouse model for studying the interaction of bisdioxopiperazines with topoisomerase $\text{II}\alpha$ in vivo
- AU Grauslund, Morten; Thougaard, Annemette Vinding; Fuechtbauer, Annette; Hofland, Kenneth Francis; Hjorth, Peter Hansen; Jensen, Peter B.; Sehested, Maxwell; Fuechtbauer, Ernst-Martin; Jensen, Lars H.
- SO Mol. Pharmacol. (2007), 72(4), 1003 1014 CODEN: MOPMA3
- DT Journal
- AN 6710431 BABS
- The bisdioxopiperazines such as (+)-(S)-4, 4'-propylenedi-2, 6-AB piperazinedione (dexrazoxane; ICRF-187), 1,2-bis(3,5dioxopiperazin-1-yl)ethane (ICRF-154), and 4,4'-(1,2-dimethyl-1,2-diethanediyl)bis-2,6-piperazinedione (ICRF-193) are agents that inhibit eukaryotic topoisomerase II, whereas their ring-opened hydrolysis products are strong iron chelator. The clinically approved analog ICRF-187 is a pharmacological modulator of topoisomerase II poisons such as etoposide in preclinical animal models. ICRF-187 is also used to protect against anthracycline-induced cardiomyopathy and has recently been approved as an antidote for alleviating tissue damage and necrosis after accidental anthracycline extravasation. This dual modality of bisdioxopiperazines, including ICRF-187, raises the question of whether their pharmacological in vivo effects are mediated through interaction with topoisomerase II or via their intracellular iron chelating activity. In an attempt to distinguish between these possibilities, we here present a transgenic mouse model aimed at identifying the contribution of topoisomerase $II\alpha$ to the effects of bisdioxopiperazines. A tyrosine 165 to serine mutation (Y165S) in topoisomerase ${\rm II}\alpha$, demonstrated previously to render the human ortholog of this enzyme highly resistant toward bisdioxopiperazines, was introduced at the TOP2A locus in mouse embryonic stem cells by targeted homologous recombination. These cells were used for the generation of transgenic TOP2A Y165S/+ mice, which were demonstrated to be resistant toward the general toxicity of both ICRF-187 and ICRF-193. Hematological measurements indicate that this is most likely caused by a decreased ability of these agents to induce myelosuppression in TOP2AY165S/+ mice, highlighting the role of topoisomerase $II\alpha$ in this process. The biological and pharmacological implications of these findings are discussed, and areas for further investigations are proposed.
- L3 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2007:1121923 CAPLUS
- DN 147:479990
- TI A mouse model for studying the interaction of bisdioxopiperazines with topoisomerase $\text{II}\alpha$ in vivo
- AU Grauslund, Morten; Thougaard, Annemette Vinding; Fuchtbauer, Annette; Hofland, Kenneth Francjs; Hjorth, Peter Hansen; Jensen, Peter B.; Sehested, Maxwell; Fuchtbauer, Ernst-Martin; Jensen, Lars H.
- CS Experimental Pathology Unit, Department of Pathology, Copenhagen University Hospital, Copenhagen, Den.
- SO Molecular Pharmacology (2007), 72(4), 1003-1014 CODEN: MOPMA3; ISSN: 0026-895X
- PB American Society for Pharmacology and Experimental Therapeutics
- DT Journal
- LA English
- AB The bisdioxopiperazines such as (+)-(S)-4,4'-propylenedi-2,6-piperazinedione (dexrazoxane; ICRF-187), 1,2-bis(3,5-dioxopiperazin-1-yl)ethane (ICRF-154), and 4,4'-(1,2-dimethyl-1,2-ethanediyl)bis-2,6-piperazinedione (ICRF-193) are agents that inhibit eukaryotic topoisomerase II, whereas their ring-opened hydrolysis products are strong iron chelator. The clin. approved analog ICRF-187 is a pharmacol. modulator of topoisomerase II

poisons such as etoposide in preclin. animal models. ICRF-187 is also used to protect against anthracycline-induced cardiomyopathy and has recently been approved as an antidote for alleviating tissue damage and necrosis after accidental anthracycline extravasation. This dual modality of bisdioxopiperazines, including ICRF-187, raises the question of whether their pharmacol. in vivo effects are mediated through interaction with topoisomerase II or via their intracellular iron chelating activity. an attempt to distinguish between these possibilities, the authors here present a transgenic mouse model aimed at identifying the contribution of topoisomerase $II\alpha$ to the effects of bisdioxopiperazines. A tyrosine 165 to serine mutation (Y165S) in topoisomerase $II\alpha$, demonstrated previously to render the human ortholog of this enzyme highly resistant toward bisdioxopiperazines, was introduced at the TOP2A locus in mouse embryonic stem cells by targeted homologous recombination. These cells were used for the generation of transgenic TOP2AY165S/+ mice, which were demonstrated to be resistant toward the general toxicity of both ICRF-187 and ICRF-193. Hematol. measurements indicate that this is most likely caused by a decreased ability of these agents to induce myelosuppression in TOP2AY165S/+ mice, highlighting the role of topoisomerase $II\alpha$ in this process. The biol. and pharmacol. implications of these findings are discussed, and areas for further investigations are proposed.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN
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AN 2005:1004605 CAPLUS

DN 143:279366

TI Cancer treatment with topoisomerase II inhibitor, a bisdioxypiperazine and radiation

- IN Hofland, Kenneth; Sehested, Maxwell; Kristjansen, Paul; Thougaard, Annemette; Jensen, Peter Buhl
- PA Topotarget A/S, Den.
- SO PCT Int. Appl., 28 pp. CODEN: PIXXD2
- DT Patent
- LA English

FAN.CNT 1

T 11114 • 1		PATENT NO.					KIND DA				APPLICATION NO.					DATE			
ΡI				A2 20 A3 20					WO 2005-IB670					20050302					
		W:	CN, GE,	CO, GH,	CR, GM,	CU, HR,	CZ, HU,	AU, DE, ID, LV,	DK, IL,	DM, IN,	DZ, IS,	EC, JP,	EE, KE,	EG, KG,	ES, KP,	FI, KR,	GB, KZ,	GD, LC,	
		RW:	NO, SY,	NZ, TJ,	OM, TM,	PG, TN,	PH, TR,	PL, TT, MW,	PT, TZ,	RO, UA,	RU, UG,	SC, US,	SD, UZ,	SE, VC,	SG, VN,	SK, YU,	SL, ZA,	SM, ZM,	ZW
			EE, RO,	ES, SE,	FI, SI,	FR, SK,	GB, TR,	RU, GR, BF,	HU,	IE,	IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,	
	CA	2005219034 2557857			,	A1 20050915			AU 2005-219034 CA 2005-2557857 EP 2005-708755						20050302				
			AT, IS,	BE, IT,	BG,	CH, LT,	CY,	CZ, MC,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,	
PRAI	US	2007527428 20070185124 2004-4675				A1		20070809											

WO 2005-IB670 20050302 W AB The present invention relates to a method of treatment of a tumor cell which comprises administering to a subject in need of treatment an effective amount of a topoisomerase-II poison, e.g. etoposide, in combination with a bis-dioxypiperazine, e.g. dexrazoxane, wherein said subject is further treated with radiation. ANSWER 7 OF 21 CAPLUS COPYRIGHT 2008 ACS on STN L3 AN 1997:556108 CAPLUS DN 127:145175 OREF 127:27889a Topoisomerase II poison and bisdioxypiperazine derivative combination therapy ΙN Jensen, Peter Buhl; Sehested, Maxwell Jensen, Peter Buhl, Den.; Sehested, Maxwell PAPCT Int. Appl., 52 pp. SO CODEN: PIXXD2 DT Patent LA English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. _____ ____ _____ WO 9725044 A1 19970717 WO 1997-DK13 19970110 PΙ W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 1997-2242406 A1 19970717 19970110 CA 2242406 AU 9713677 Α 19970801 AU 1997-13677 19970110 EP 1997-900205 EP 874630 Α1 19981104 19970110 EP 874630 20030820 В1 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI AT 247468 20030915 AT 1997-900205 19970110 PT 874630 Τ 20040130 PT 1997-900205 19970110 T3 20040501 B1 20010724 ES 2205164 ES 1997-900205 19970110 US 6265385 US 1999-101499 19990308 PRAI DK 1996-22 А 19960111 US 1996-603105 Α 19960220 WO 1997-DK13 W 19970110 The present invention relates to a method for selectively killing tumor or AB metastatic cells within a defined compartment of the organism of a large mammal, in particular a human, said method comprising administering to a mammal an effective tumor- or metastasis-killing amount of a topoisomerase II poison except doxorubicin, and protecting non-tumorous tissue of the mammal against the toxic action of the topoisomerase II poison by administration of a bis-dioxypiperazine compound In particular, the invention relates to a pharmaceutical kit for selectively killing tumor or metastatic cells within the central nervous system of a large mammal, in particular a human, said kit comprising: a) a dosage unit of a bis-dioxypiperazine and a pharmaceutically acceptable carrier, and b) a dosage unit of topoisomerase II poisons except doxorubicin and a pharmaceutically acceptable carrier.

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11535037 IFIPAT; IFIUDB; IFICDB
ΑN
      Cancer treatment with topoisomerase-ii inhibitor, a bis-
ΤТ
      dioxypiperazine and radiation
      Hofland; Kenneth, Copenhagen, DK
INF
      Sehested; Maxwell, Copenhagen, DK
      Kristjansen; Paul, Copenhagen, DK
      Thougaard; Annenette, Copenhagen, DK
      Jensen; Peter Buhl, Copenhagen, DK
ΙN
      Hofland Kenneth (DK); Jensen Peter Buhl (DK); Kristjansen Paul (DK);
      Sehested Maxwell (DK); Thougaard Annenette (DK)
      Unassigned
PAF
      Unassigned Or Assigned To Individual (68000)
PΑ
PPA
      Topotarget A S DK (Probable)
ΑG
      NIXON & VANDERHYE, PC, 901 NORTH GLEBE ROAD, 11TH FLOOR, ARLINGTON, VA,
      22203, US
PΙ
      US 20070185124 A1 20070809
      US 2005-591847
ΑI
                          20050302
      WO 2005-IB670
                          20050302
                          20070109 PCT 371 date
                          20070109 PCT 102(e) date
PRAI GB 2004-46751
                           20040302
FI
      US 20070185124
                          20070809
DT
      Utility; Patent Application - First Publication
FS
      CHEMICAL
      APPLICATION
      Entered STN: 10 Aug 2007
ED
      Last Updated on STN: 13 Sep 2007
CLMN
AΒ
      The present invention relates to a method of treatment of a tumour cell
      which comprises administering to a subject in need of treatment an
      effective amount of a topoisomerase-II poison
      , e.g. etoposide, in combination with a bis-dioxypiperazine,
      e.g. dexrazoxane wherein said subject is further treated with radiation.
CLMN
     10
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     ANSWER 9 OF 21 IFIPAT COPYRIGHT 2008 IFI on STN
ΑN
      03547524 IFIPAT; IFIUDB; IFICDB
      TOPOISOMERASE II POISON AND
TΙ
      BIS-DIOXOPIPERAZINE DERIVATIVE COMBINATION THERAPY; SELECTIVELY KILLING
      TUMOR OR METASTATIC CELLS WITHIN A DEFINED COMPARTMENT OF A HUMAN;
      TOPOISOMERASE II POISON IS ETOPOSIDE OR
      TENIPOSIDE AND WHERE SAID BIS-DIOXOPIPERAZINE IS (+)-1,2-BIS(3,5-
      DIOXOPIPERAZINYL-1-YL) PROPANE
INF
      Jensen; Peter Buhl, Farum, DK
      Sehested; Maxwell, Kobenhavn O, DK
      Jensen Peter Buhl (DK); Sehested Maxwell (DK)
ΤN
PAF
      Topo Target ApS, Copenhagen, DK
      Topo Target ApS DK (57956)
PA
EXNAM Geist, Gary
EXNAM Crane, L. E
ΑG
      Cooper, Iver P.
PΙ
      US 6265385
                      В1
                          20010724
      WO 9725044
                          19970717
      US 1999-101499
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                          19990308
      WO 1997-DK13
                          19970110
                          19990308 PCT 371 date
                          19990308 PCT 102(e) date
      10 Jan 2017
XPD
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FI
      US 6265385
                          20010724
DT
      Utility; Reassigned
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CHEMICAL FS GRANTED Entered STN: 26 Jul 2001 EDLast Updated on STN: 8 Jul 2002 MFN: 0172 MRN 011670 011670 0179 CLMN 54 GΙ 1 Drawing Sheet(s), 1 Figure(s). AΒ The present invention relates to a method for selectively killing tumor or metastatic cells within a defined compartment of the organism of a large mammal, in particular a human, said method comprising administering to a mammal an effective tumor-or metastasis-killing amount of a topoisomerase II poison except doxorubicin, and protecting non-tumorous tissue of the mammal against the toxic action of the topoisomerase II poison by administration of a bis-dioxypiperazine compound. In particular, the invention relates to a pharmaceutical kit for selectively killing tumor or metastatic cells within the central nervous system in a large mammal, in particular a human, said kit comprising: a) a dosage unit of a bis-dioxypiperazine and a pharmaceutically acceptable carrier, and b) a dosage unit of topoisomerase II poisons except doxorubicin and a pharmaceutically acceptable carrier. CLMN GΙ 1 Drawing Sheet(s), 1 Figure(s). ANSWER 10 OF 21 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on L3 STN ΑN 2007:1060925 SCISEARCH The Genuine Article (R) Number: 211YZ GΑ ΤI A mouse model for studying the interaction of bisdioxopiperazines with topoisomerase II alpha in vivo Grauslund, Morten; Thougaard, Annemette Vinding; Fuechtbauer, Annette; ΑU Hofland, Kenneth Francis; Hjorth, Peter Hansen; Jensen, Peter B.; Sehested, Maxwell; Fuechtbauer, Ernst-Martin; Jensen, Lars H. (Reprint) CS Rigshosp, Dept Pathol, Expt Pathol Unit, Bioctr, Bygning 2, 3 Sal, Ole Maaloes Vej 5, DK-2100 Copenhagen O, Denmark (Reprint); Univ Copenhagen Hosp, Dept Pathol, Expt Pathol Unit, DK-2100 Copenhagen, Denmark; Topo Target AS, Copenhagen, Denmark; Univ Aarhus, Dept Mol Biol, Aarhus, Denmark; Univ Copenhagen Hosp, Finsen Ctr, Lab Expt Med Oncol, DK-2100 Copenhagen, Denmark lhj@topotarget.com CYA Denmark MOLECULAR PHARMACOLOGY, (OCT 2007) Vol. 72, No. 4, pp. 1003-1014. SO ISSN: 0026-895X. AMER SOC PHARMACOLOGY EXPERIMENTAL THERAPEUTICS, 9650 ROCKVILLE PIKE, PB BETHESDA, MD 20814-3995 USA. Article; Journal DT LA English REC Reference Count: 40 EDEntered STN: 18 Oct 2007 Last Updated on STN: 18 Oct 2007 *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS* The bisdioxopiperazines such as (+)-(S)-4,4 '-propylenedi-2,6-AΒ piperazinedione (dexrazoxane; ICRF-187), 1,2-bis(3,5dioxopiperazin1- yl) ethane (ICRF-154), and 4,4 '-(1,2-dimethyl-1,2ethanediyl) bis-2,6-piperazinedione (ICRF-193) are agents that inhibit eukaryotic topoisomerase II, whereas their ring-opened hydrolysis products are strong iron chelator. The clinically approved analog ICRF-187 is a pharmacological modulator of topoisomerase II

poisons such as etoposide in preclinical animal models. ICRF- 187

is also used to protect against anthracyclineinduced cardiomyopathy and has recently been approved as an antidote for alleviating tissue damage and necrosis after accidental anthracycline extravasation. This dual modality of bisdioxopiperazines, including ICRF- 187, raises the question of whether their pharmacological in vivo effects are mediated through interaction with topoisomerase II or via their intracellular iron chelating activity. In an attempt to distinguish between these possibilities, we here present a transgenic mouse model aimed at identifying the contribution of topoisomerase II alpha to the effects of bisdioxopiperazines. A tyrosine 165 to serine mutation (Y165S) in topoisomerase II alpha, demonstrated previously to render the human ortholog of this enzyme highly resistant toward bisdioxopiperazines, was introduced at the TOP2A locus in mouse embryonic stem cells by targeted homologous recombination. These cells were used for the generation of transgenic TOP2A(Y165S/+) mice, which were demonstrated to be resistant toward the general toxicity of both ICRF-187 and ICRF-193. Hematological measurements indicate that this is most likely caused by a decreased ability of these agents to induce myelosuppression in TOP2A(Y165S/+) mice, highlighting the role of topoisomerase II alpha in this process. The biological and pharmacological implications of these findings are discussed, and areas for further investigations are proposed.

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ANSWER 11 OF 21 USPATFULL on STN
L3
       2007:224264 USPATFULL
ΑN
TΙ
       SUCCINIMIDE AND MALEIMIDE DERIVATIVES AND THEIR USE AS TOPOISOMERASE II
       CATALYTIC INHIBITORS
       Jensen, Peter Buhl, Farum, DENMARK
ΙN
       Sokilde, Birgitte, Vaerlose, DENMARK
       Carstensen, Elisabeth Vang, Farum, DENMARK
       Langer, Seppo W., Gentofte, DENMARK
       Creighton, Andrew, London, UNITED KINGDOM
       Sehested, Maxvell, Copenhagen, DENMARK
       Jensen, Lars Hollund, Valby, DENMARK
PA
       TOPOTARGET A/S (non-U.S. corporation)
PΙ
       US 20070196360
                          A1 20070823
ΑI
      US 2006-557631
                          A1 20061108 (11)
      Continuation of Ser. No. US 2002-108979, filed on 29 Mar 2002, ABANDONED
RLI
PRAI
       DK 2001-522
                           20010329
       US 2001-279459P
                           20010329 (60)
DT
       Utility
FS
      APPLICATION
LREP
      FOLEY AND LARDNER LLP, SUITE 500, 3000 K STREET NW, WASHINGTON, DC,
       20007, US
CLMN
      Number of Claims: 3
      Exemplary Claim: 1-47
ECL
DRWN
      11 Drawing Page(s)
LN.CNT 1838
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      Maleimide and succinimide derivatives were found to be effective
AB
       topoisomerase II catalytic inhibitors. Due to this property, the
       maleimide and succinimide derivatives were investigated for their use as
       cytostatic agents and thus in the treatment of cancer. The compounds of
       the invention can be used in combination treatments with other
       cytostatic agents, such as topoisomerase II
       poisons. The maleimide and succinimide derivatives, due to their
       effective topoisomerase II catalytic inhibitory activity, are also
       useful as extravasation agents, such as upon administration of a
       topoisomerase II poison.
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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ANSWER 12 OF 21 USPATFULL on STN
T.3
       2007:211316 USPATFULL
ΑN
ΤТ
       Cancer treatment with topoisomerase-ii inhibitor, a bis-
       dioxypiperazine and radiation
       Hofland, Kenneth, Copenhagen, DENMARK
TN
       Sehested, Maxwell, Copenhagen, DENMARK
       Kristjansen, Paul, Copenhagen, DENMARK
       Thougaard, Annenette, Copenhagen, DENMARK
       Jensen, Peter Buhl, Copenhagen, DENMARK
PΙ
       US 20070185124
                           A1 20070809
ΑI
       US 2005-591847
                           A1 20050302 (10)
       WO 2005-IB670
                               20050302
                               20070109 PCT 371 date
PRAI
       GB 2004-4675
                           20040302
DT
       Utility
FS
       APPLICATION
       NIXON & VANDERHYE, PC, 901 NORTH GLEBE ROAD, 11TH FLOOR, ARLINGTON, VA,
LREP
       22203, US
       Number of Claims: 10
CLMN
ECL
       Exemplary Claim: 1
DRWN
       2 Drawing Page(s)
LN.CNT 681
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention relates to a method of treatment of a tumour cell
       which comprises administering to a subject in need of treatment an
       effective amount of a topoisomerase-II
       poison, e.g. etoposide, in combination with a bis-
       dioxypiperazine, e.g. dexrazoxane wherein said subject is
       further treated with radiation.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 13 OF 21 USPATFULL on STN
T.3
       2007:36275 USPATFULL
ΑN
ΤI
       Screening method for identifying hsp90 modulators
ΤN
       Jenkins, John, Liverpool, UNITED KINGDOM
       Greenhalf, William, Liverpool, UNITED KINGDOM
       O'Connor, David Ian, Staffordshire, UNITED KINGDOM
       University of Liverpool, Liverpool, UNITED KINGDOM, L69 3BX (non-U.S.
PA
       corporation)
PΙ
       US 20070031815
                           A1 20070208
ΑI
       US 2004-554973
                           A1 20040428 (10)
       WO 2004-GB1828
                               20040428
                               20051031 PCT 371 date
       GB 2003-10017
                           20030501
PRAI
       Utility
DТ
FS
       APPLICATION
       DAVIS WRIGHT TREMAINE LLP, 865 FIGUEROA STREET, SUITE 2400, LOS ANGELES,
LREP
       CA, 90017-2566, US
       Number of Claims: 20
CLMN
ECL
       Exemplary Claim: 1
DRWN
       6 Drawing Page(s)
LN.CNT 962
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A screening method for identifying and/or analysing Hsp90 inhibitors
       and/or Hsp90 agonists comprises the steps of contacting a compound with
       at least two of yeast strains A-E wherein each yeast strain comprises
       expression vectors from which a pair of binding partners for a yeast
       two-hybrid assay are expressed. The binding partner pairs comprise: A:
       Hsp90-targeting protein; B: Hsp90-Hsp90; C: Hsp90-p23; D: Hsp90-E3
       ligase; E: Hsp90-Client. Inhibition and/or promotion of dimerisation
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between the binding partners is then measured.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 14 OF 21 USPATFULL on STN L3 2006:282242 USPATFULL ΑN TΙ Alkylating agent combinations in the treatment of cancer INGerson, Stanton L., Huntington Valley, OH, UNITED STATES Liu, Lili, Northfield, OH, UNITED STATES PΙ US 20060241186 A1 20061026 US 2003-505400 A1 20030219 (10) ΑI WO 2003-US5032 20030219 20050622 PCT 371 date Continuation of Ser. No. US 2002-79049, filed on 19 Feb 2002, GRANTED, RLI Pat. No. US 6635677 Continuation-in-part of Ser. No. US 1999-373693, filed on 13 Aug 1999, GRANTED, Pat. No. US 6465448 DТ Utility FS APPLICATION FISH & NEAVE IP GROUP, ROPES & GRAY LLP, ONE INTERNATIONAL PLACE, LREP BOSTON, MA, 02110-2624, US CLMN Number of Claims: 43 ECL Exemplary Claim: 1 24 Drawing Page(s) DRWN LN.CNT 2099 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This application provides compositions and methods useful in the treatment of certain cancers. In part, this application is based on the recognition that certain molecules that target abasic lesions or AP sites in DNA improve, augment, or potentiate the chemotherapeutic efficacy of certain anticancer agents. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 15 OF 21 USPATFULL on STN L3 2003:45313 USPATFULL ΑN TΤ Succinimide and maleimide derivatives and their use as topoisomerase II catalytic inhibitors Jensen, Peter Buhl, Farum, DENMARK Sokilde, Birgitte, Vaerlose, DENMARK Carstensen, Elisabeth Vang, Farum, DENMARK Langer, Seppo W., Gentofte, DENMARK Creighton, Andrew, London, UNITED KINGDOM Sehested, Maxvell, Copenhagen, DENMARK Jensen, Lars Hollund, Valby, DENMARK PΑ Topo Target ApS, Copenhagen, DENMARK (non-U.S. corporation) РΤ US 20030032625 A1 20030213 US 2002-108979 ΑI A1 20020329 (10) DK 2001-522 20010329 PRAI US 2001-279459P 20010329 (60) DT Utility FS APPLICATION BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, LREP WASHINGTON, DC, 20001-5303 Number of Claims: 48 CLMN Exemplary Claim: 1 ECL 11 Drawing Page(s) DRWN LN.CNT 2174 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AΒ Maleimide and succinimide derivatives were found to be effective

topoisomerase II catalytic inhibitors. Due to this property, the

maleimide and succinimide derivatives were investigated for their use as

cytostatic agents and thus in the treatment of cancer. The compounds of the invention can be used in combination treatments with other cytostatic agents, such as topoisomerase II poisons. The maleimide and succinimide derivatives, due to their effective topoisomerase II catalytic inhibitory activity, are also useful as extravasation agents, such as upon administration of a topoisomerase II poison.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L3
     ANSWER 16 OF 21 USPATFULL on STN
ΑN
       2002:186136 USPATFULL
ΤI
       Treatment of accidental extravasation of anthracyclines
ΙN
       Langer, Seppo W., Gentofte, DENMARK
       Jensen, Peter B., Farum, DENMARK
       Sehested, Maxwell, Copenhagen, DENMARK
       US 20020099057
                           A1 20020725
PΙ
       US 6727253
                           B2 20040427
       US 2001-893521
                           A1 20010629 (9)
ΑI
       Continuation-in-part of Ser. No. WO 2000-DK107, filed on 13 Mar 2000,
RLT
       UNKNOWN
PRAI
       DK 1999-355
                           19990312
       Utility
DT
FS
       APPLICATION
LREP
       BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300,
       WASHINGTON, DC, 20001-5303
      Number of Claims: 51
CLMN
ECL
       Exemplary Claim: 1
DRWN
       12 Drawing Page(s)
LN.CNT 1375
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The present invention relates to a method and a medicament for
       pharmacological treatment of accidental extravasation of
       topoisomerase II poisons such as
       anthracyclines. In particular, the invention relates to the use of a
       topo II catalytic nhibitor such as the bisdioxopiperazine ICRF-187 for
       the manufacture of a medicament for the treatment of an accidental
       extravasation of a topoisomerase II poison
       and a method for treatment of such extravasation of a topoisomerase
       poison such as the anthracyclines daunorubicin, doxorubicin, epirubicin,
       or idarubicin. In addition, the invention relates to a kit for such
       treatment.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
T.3
     ANSWER 17 OF 21 USPATFULL on STN
       2001:116991 USPATFULL
```

```
ΑN
       Topoisomerase II poison and
TΙ
       bis-dioxopiperazine derivative combination therapy
       Jensen, Peter Buhl, Farum, Denmark
ΙN
       Sehested, Maxwell, K.o slashed.benhavn .O slashed., Denmark
       Topo Target ApS, Copenhagen, Denmark (non-U.S. corporation)
PA
PΙ
       US 6265385
                           B1 20010724
       WO 9725044 19970717
       US 1999-101499
                               19990308 (9)
ΑТ
       WO 1997-DK13
                               19970110
                               19990308 PCT 371 date
                               19990308 PCT 102(e) date
PRAI
       DK 1996-22
                           19960111
       Utility
DT
FS
       GRANTED
```

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EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: Crane, L. E.
      Cooper, Iver P.
LREP
      Number of Claims: 54
CLMN
       Exemplary Claim: 1,12,43
ECL
DRWN
       1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1373
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to a method for selectively killing tumor
AB
       or metastatic cells within a defined compartment of the organism of a
       large mammal, in particular a human, said method comprising
       administering to a mammal an effective tumor--or metastasis-killing
       amount of a topoisomerase II poison except
       doxorubicin, and protecting non-tumorous tissue of the mammal against
       the toxic action of the topoisomerase II
       poison by administration of a bis-dioxypiperazine
       compound. In particular, the invention relates to a pharmaceutical kit
       for selectively killing tumor or metastatic cells within the central
       nervous system in a large mammal, in particular a human, said kit
       comprising: a) a dosage unit of a bis-dioxypiperazine and a
       pharmaceutically acceptable carrier, and b) a dosage unit of
       topoisomerase II poisons except doxorubicin
       and a pharmaceutically acceptable carrier.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 18 OF 21 USPAT2 on STN
T.3
       2002:186136 USPAT2
ΑN
ΤТ
       Treatment of accidental extravasation of anthracyclines
IN
       Langer, Seppo W., Gentofte, DENMARK
       Jensen, Peter B., Farum, DENMARK
       Sehested, Maxwell, Copenhagen, DENMARK
PΑ
       Antianthra APS, Farum, DENMARK (non-U.S. corporation)
PΙ
      US 6727253
                          B2 20040427
      US 2001-893521
                               20010629 (9)
AΙ
RLI
      Continuation-in-part of Ser. No. WO 2000-DK107, filed on 13 Mar 2000
PRAI
      DK 1999-355
                          19990312
DT
      Utility
      GRANTED
EXNAM Primary Examiner: Spivack, Phyllis G.
LREP
      Cooper, Iver P.
      Number of Claims: 31
CLMN
ECL
      Exemplary Claim: 1
      12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 1327
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       The present invention relates to a method for pharmacological treatment
       of accidental extravasation of topoisomerase II
       poisons, such as anthracyclines. In particular, the invention
       relates to the use of a topo II catalytic inhibitor, such as the
       bisdioxopiperazine ICRF-187, for the treatment of an accidental
       extravasation of a topoisomerase II poison
       . A method for treatment of such extravasation of a topoisomerase poison
       such as the anthracyclines, daunorubicin, doxorubicin, epirubicin, or
       idarubicin is disclosed.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L3
    ANSWER 19 OF 21 WPINDEX COPYRIGHT 2008
                                                   THOMSON REUTERS on STN
AN
    1997-372598 [34] WPINDEX
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Selective killing of tumour or metastatic cells - using

DNC C1997-120018 [34]

ΤТ

```
topoisomerase II poison except doxorubicin and
     bis-dioxypiperazine compound to protect non-tumourous tissue
DC
    B03; B05
ΙN
     JENSEN P; JENSEN P B; LENSEN P B; SEHESTED M
     (JENS-I) JENSEN P; (JENS-I) JENSEN P B; (SEHE-I) SEHESTED M; (TOPO-N) TOPO
PA
     TARGET APS; (TOPO-N) TOPOTARGET APS
CYC 72
PIA WO 9725044
                    A1 19970717 (199734)* EN
                                              53[1]
    AU 9713677
                    A 19970801 (199748) EN
     EP 874630
                   A1 19981104 (199848) EN
     US 6265385
                    B1 20010724 (200146) EN
     EP 874630
                   B1 20030820 (200356) EN
     DE 69724228
                   E 20030925 (200371) DE
                    T3 20040501 (200431) ES
     ES 2205164
ADT WO 9725044 A1 WO 1997-DK13 19970110; AU 9713677 A AU 1997-13677 19970110;
     DE 69724228 E DE 1997-69724228 19970110; EP 874630 A1 EP 1997-900205
     19970110; EP 874630 B1 EP 1997-900205 19970110; DE 69724228 E EP
     1997-900205 19970110; ES 2205164 T3 EP 1997-900205 19970110; AU 9713677 A
     WO 1997-DK13 19970110; EP 874630 A1 WO 1997-DK13 19970110; US 6265385 B1
     WO 1997-DK13 19970110; EP 874630 B1 WO 1997-DK13 19970110; DE 69724228 E
     WO 1997-DK13 19970110; US 6265385 B1 US 1999-101499 19990308
    DE 69724228 E Based on EP 874630 A; ES 2205164 T3 Based on EP 874630 A; AU
     9713677 A Based on WO 9725044 A; EP 874630 A1 Based on WO 9725044 A; US
     6265385 B1 Based on WO 9725044 A; EP 874630 B1 Based on WO 9725044 A; DE
     69724228 E Based on WO 9725044 A
PRAI US 1996-603105
                          19960220
     DK 1996-22
                          19960111
ΑN
     1997-372598 [34]
                       WPINDEX
AΒ
    WO 1997025044 A1
                       UPAB: 20050703
    Method for selectively killing tumour or metastatic cells within a
     compartment of the organism of a large mammal, in particular a human,
     comprises administering a topoisomerase II
     poison (T II P) except doxorubicin, and protecting non-tumourous
     tissue of the mammal against the toxic action of the T II P by
     administration of a bis-dioxypiperazine compound (BDC).
     Also claimed is a kit for selectively killing tumour or metastatic cells
     within the central nervous system (CNS) of a large mammal, particularly a
     human, comprising:
     (a) a dosage unit of a BDC and a carrier, and
     (b) a dosage unit of T II P except doxorubicin and a carrier.
           USE - The method can be used for selectively killing tumour or
     metastatic cells, particularly in the CNS of humans (all claimed).
           ADVANTAGE - Using the method the normal tissue is protected from the
     poison by the bis-dioxypiperazine whereby the malignant
     conditions can be treated with higher dosages of the T II P and side
     effects are reduced.
Member (0003)
ABEQ EP 874630 A1
                   UPAB 20050703
     Method for selectively killing tumour or metastatic cells within a
     compartment of the organism of a large mammal, in particular a human,
     comprises administering a topoisomerase II
     poison (T II P) except doxorubicin, and protecting non-tumourous
     tissue of the mammal against the toxic action of the T II P by
     administration of a bis-dioxypiperazine compound (BDC).
     Also claimed is a kit for selectively killing tumour or metastatic cells
     within the central nervous system (CNS) of a large mammal, particularly a
     human, comprising:
     (a) a dosage unit of a BDC and a carrier, and
     (b) a dosage unit of T II P except doxorubicin and a carrier.
```

USE - The method can be used for selectively killing tumour or

metastatic cells, particularly in the CNS of humans (all claimed).

ADVANTAGE - Using the method the normal tissue is protected from the poison by the bis-dioxypiperazine whereby the malignant conditions can be treated with higher dosages of the T II P and side effects are reduced.

Member (0004)

ABEQ US 6265385 B1 UPAB 20050703

Method for selectively killing tumour or metastatic cells within a compartment of the organism of a large mammal, in particular a human, comprises administering a topoisomerase II poison (T II P) except doxorubicin, and protecting non-tumourous

poison (T II P) except doxorubicin, and protecting non-tumourous tissue of the mammal against the toxic action of the T II P by administration of a bis-dioxypiperazine compound (BDC).

Also claimed is a kit for selectively killing tumour or metastatic cells within the central nervous system (CNS) of a large mammal, particularly a human, comprising:

- (a) a dosage unit of a BDC and a carrier, and
- (b) a dosage unit of T II P except doxorubicin and a carrier.

USE - The method can be used for selectively killing tumour or metastatic cells, particularly in the CNS of humans (all claimed).

ADVANTAGE - Using the method the normal tissue is protected from the poison by the bis-dioxypiperazine whereby the malignant conditions can be treated with higher dosages of the T II P and side effects are reduced.

- L3 ANSWER 20 OF 21 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
- AN 2008097296 EMBASE
- TI Mutagenicity of some topoisomerase II-interactive agents.
- AU Attia, Sabry M. (correspondence)
- CS Department of Pharmacology, College of Pharmacy, King Saud University, PO Box 2457, Riyadh 11451, Saudi Arabia. attiasm@yahoo.com
- SO Saudi Pharmaceutical Journal, (Jan 2008) Vol. 16, No. 1, pp. 1-24. Refs: 207
 - ISSN: 1319-0164 CODEN: SPJOEM
- CY Saudi Arabia
- DT Journal; General Review; (Review)
- FS 016 Cancer
 - 017 Public Health, Social Medicine and Epidemiology
 - 022 Human Genetics
 - 037 Drug Literature Index
 - 038 Adverse Reactions Titles
- LA English
- SL English; Arabic
- ED Entered STN: 4 Apr 2008
 - Last Updated on STN: 4 Apr 2008
- AB Among the anticancer drugs currently used in the treatment of human malignancies, as well as several new series of drugs under development, are targeted at topoisomerase II enzymes. Besides of inducing cell death due to both 'mitotic catastrophe' and the induction of apoptosis, topoisomerase-II-targeted drugs can increase the frequency of cells bearing mutations. These cells can develop resistance to the therapeutic agents or may lead to the development of secondary tumours and abnormal reproductive outcomes. This review focuses on the mutagenic properties of the topoisomerase II poisons etoposide,

doxorubicin and amsacrine, which are front-line therapies for a variety of malignancies, and genistein, which is prominent in soybean foods and is believed to be a chemopreventative agent that contributes to the low incidence of specific cancers among Asian populations. In addition, the topoisomerase II catalytic inhibitor merbarone that is in clinical trials

as an anticancer agent will be discussed. It clear from the present review that, the topoisomerase II-interactive anticancer agents appear to be mutagenic. Therefore, the clinical use of these mutagenic drugs must be weighed against the risks of secondary malignancies in cured patients and persistent genetic damage of their potential offspring.

- L3 ANSWER 21 OF 21 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
- AN 2007472968 EMBASE
- TI A mouse model for studying the interaction of bisdioxopiperazines with topoisomerase $\text{II}\alpha$ in vivo.
- AU Grauslund, Morten; Sehested, Maxwell; Jensen, Lars H., Dr. (correspondence)
- CS Experimental Pathology Unit, Department of Pathology, Copenhagen University Hospital, Copenhagen, Denmark. lhj@topotarget.com
- AU Grauslund, Morten; Thougaard, Annemette Vinding; Hofland, Kenneth Francis; Jensen, Peter B.; Sehested, Maxwell; Jensen, Lars H., Dr. (correspondence)
- CS TopoTarget A/S, Copenhagen, Denmark. lhj@topotarget.com
- AU Fuchtbauer, Annette; Hjorth, Peter Hansen; Fuchtbauer, Ernst-Martin
- CS Department of Molecular Biology, University of Aarhus, Aarhus, Denmark.
- AU Jensen, Peter B.
- CS Laboratory for Experimental Medical Oncology, Finsen Center, Copenhagen University Hospital, Copenhagen, Denmark.
- AU Jensen, Lars H., Dr. (correspondence)
- CS Department of Pathology, Rigshospitalet Afs. 3731, Biocenter, Bygning 2, 3 sal., Ole Maales vej 5, DK-2100 Copenhagen O, Denmark. lhj@topotarget.com
- SO Molecular Pharmacology, (Oct 2007) Vol. 72, No. 4, pp. 1003-1014. Refs: 40
 - ISSN: 0026-895X E-ISSN: 1521-0111 CODEN: MOPMA3
- CY United States
- DT Journal; Article
- FS 030 Clinical and Experimental Pharmacology 037 Drug Literature Index Toxicology
- LA English
- SL English
- ED Entered STN: 11 Oct 2007 Last Updated on STN: 11 Oct 2007
- AΒ The bisdioxopiperazines such as (+)-(S)-4, 4'-propylenedi-2, 6piperazinedione (dexrazoxane; ICRF-187), 1,2-bis(3,5dioxopiperazin-1-y1) ethane (ICRF-154), and 4,4'-(1,2-dimethy1-1,2ethanediyl)bis-2,6-piperazinedione (ICRF-193) are agents that inhibit eukaryotic topoisomerase II, whereas their ring-opened hydrolysis products are strong iron chelator. The clinically approved analog ICRF-187 is a pharmacological modulator of topoisomerase II poisons such as etoposide in preclinical animal models. ICRF-187 is also used to protect against anthracycline-induced cardiomyopathy and has recently been approved as an antidote for alleviating tissue damage and necrosis after accidental anthracycline extravasation. This dual modality of bisdioxopiperazines, including ICRF-187, raises the question of whether their pharmacological in vivo effects are mediated through interaction with topoisomerase II or via their intracellular iron chelating activity. In an attempt to distinguish between these possibilities, we here present a transgenic mouse model aimed at identifying the contribution of topoisomerase $II\alpha$ to the effects of bisdioxopiperazines. A tyrosine 165 to serine mutation (Y165S) in topoisomerase ${\rm II}\alpha$, demonstrated previously to render the human ortholog of this enzyme highly resistant toward bisdioxopiperazines, was introduced at the TOP2A locus in mouse embryonic stem cells by targeted homologous recombination. These cells were used for the generation of transgenic TOP2A (Y165S/+) mice, which were demonstrated to be resistant

toward the general toxicity of both ICRF-187 and ICRF-193. Hematological measurements indicate that this is most likely caused by a decreased ability of these agents to induce myelosuppression in TOP2A(Y165S/+) mice, highlighting the role of topoisomerase II α in this process. The biological and pharmacological implications of these findings are discussed, and areas for further investigations are proposed. Copyright .COPYRGT. 2007 The American Society for Pharmacology and Experimental Therapeutics.

```
=> s piperazinedione(w)radiation
             1 PIPERAZINEDIONE(W) RADIATION
=> dis 14 bib abs
     ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
T.4
     1977:113324 CAPLUS
ΑN
     86:113324
DN
OREF 86:17827a,17830a
     An ENDOR study of the \delta proton hyperfine interaction in x-ray
ТΤ
     damaged 2,5-piperazinedione
ΑU
     Helms, H. A., Jr.; Miyagawa, Ichiro
CS
     Dep. Phys. Astron., Univ. Alabama, University, AL, USA
SO
     Journal of Chemical Physics (1976), 65(9), 3493-4
     CODEN: JCPSA6; ISSN: 0021-9606
     Journal
DT
     English
LA
AΒ
     ENDOR studies of x-ray irradiated crystals of 2,5-piperazinedione were
     conducted. The structure of the primary radical reported in the previous
     ESR studies was confirmed, but anal. of the \delta proton hfs tensors
     showed that neither of the previously proposed models for hfs of the
     \delta proton is correct. The present results indicate that practically
     all of the spin d. must be in the vicinity of the \alpha C.
=> s piperazinedione
          5385 PIPERAZINEDIONE
=> s 15 and radiation
           786 L5 AND RADIATION
=> s 16 and (anti(a)tumor)
T.7
           455 L6 AND (ANTI(A) TUMOR)
=> s 17 and toxicity
           433 L7 AND TOXICITY
L8
\Rightarrow s 18 and bis
           394 L8 AND BIS
L9
=> s (bis and ethanediyl)
L10
          6550 (BIS AND ETHANEDIYL)
=> s 18 and (bis and ethanediyl)
            67 L8 AND (BIS AND ETHANEDIYL)
=> s 111 and ionizing
L12
            59 L11 AND IONIZING
=> dis 112 1-59 bib abs
```

```
L12 ANSWER 1 OF 59 USPATFULL on STN
       2008:152188 USPATFULL
ΑN
ΤТ
       Conformationally Constrained Smac Mimetics And The Uses Thereof
ΙN
       Wang, Shaomeng, Saline, MI, UNITED STATES
       Sun, Haiying, Ann Arbor, MI, UNITED STATES
       Nikolovksa-Coleska, Zaneta, Ann Arbor, MI, UNITED STATES
       Yang, Chao-Yie, Ann Arbor, MI, UNITED STATES
       Xu, Liang, Ann Arbor, MI, UNITED STATES
       Saito, Naoyuki G., East Amherst, NY, UNITED STATES
       Chen, Jianyong, Ann Arbor, MI, UNITED STATES
PΙ
       US 20080132485
                           A1 20080605
ΑI
       US 2005-632079
                           A1 20050711 (11)
       WO 2005-US24530
                               20050711
                               20080220 PCT 371 date
       US 2004-586575P
                           20040709 (60)
PRAT
       Utility
DT
       APPLICATION
FS
LREP
       MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA,
       94105, US
       Number of Claims: 48
CLMN
ECL
       Exemplary Claim: 1
DRWN
       35 Drawing Page(s)
LN.CNT 2751
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to conformationally constrained mimetics of Smac
       which function as inhibitors of Inhibitor of Apoptosis Proteins. The
       invention also relates to the use of these mimetics for inducing
       apoptotic cell death and for sensitizing cells to inducers of apoptosis.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 2 OF 59 USPATFULL on STN
       2008:103430 USPATFULL
ΑN
       Bivalent SMAC mimetics and the uses thereof
ΤI
       Wang, Shaomeng, Saline, MI, UNITED STATES
ΙN
       Sun, Haiying, Ann Arbor, MI, UNITED STATES
       Qin, Dongguang, Ann Arbor, MI, UNITED STATES
       Nikolovska-Coleska, Zaneta, Ann Arbor, MI, UNITED STATES
       Lu, Jianfeng, Ann Arbor, MI, UNITED STATES
       Qiu, Su, Ann Arbor, MI, UNITED STATES
       Peng, Yuefeng, Ann Arbor, MI, UNITED STATES
PΑ
       Regents of the University of Michigan, Ann Arbor, MI, UNITED STATES
       (U.S. corporation)
PΙ
       US 20080089896
                           A1 20080417
       US 2007-800220
                           A1 20070504 (11)
ΑТ
                           20070413 (60)
PRAI
       US 2007-923415P
       US 2006-798018P
                           20060505 (60)
DT
       Utility
FS
       APPLICATION
       MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA,
LREP
       94105, US
       Number of Claims: 61
CLMN
ECL
       Exemplary Claim: 1
       6 Drawing Page(s)
DRWN
LN.CNT 3298
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to bivalent mimetics of Smac which function as
       inhibitors of Inhibitor of Apoptosis Proteins. The invention also
       relates to the use of these mimetics for inducing apoptotic cell death
       and for sensitizing cells to inducers of apoptosis.
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

```
L12 ANSWER 3 OF 59 USPATFULL on STN
ΑN
       2006:328918 USPATFULL
ТΤ
       Electrical devices and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20060282123
                           A1 20061214
ΑI
       US 2004-6910
                           A1 20041207 (11)
RLI
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
       US 2004-586861P
PRAI
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
ECL
       Exemplary Claim: 1-2264
DRWN
       32 Drawing Page(s)
LN.CNT 14774
AΒ
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
L12 ANSWER 4 OF 59 USPATFULL on STN
       2006:174046 USPATFULL
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20060147492
                           A1 20060706
ΑI
       US 2006-343809
                           A1 20060131 (11)
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
RLI
                           20040709 (60)
PRAI
       US 2004-586861P
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
                           20031120 (60)
       US 2003-523908P
       US 2003-524023P
                           20031120 (60)
       US 2003-518785P
                           20031110 (60)
       Utility
DT
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
```

Number of Claims: 52 CT.MN Exemplary Claim: 1 ECL 28 Drawing Page(s) DRWN LN.CNT 56233 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Implants are used in combination with an anti-scarring agent in order to AB inhibit scarring that may otherwise occur when the implant is placed within an animal. The agent may be any suitable anti-scarring agent, e.g., a cell cycle inhibitor, and may be used in conjunction with a second pharmaceutical agent, e.g., an antibiotic. Suitable implants include intravascular implants, a vascular graft or wrap implant, an implant for hemodialysis access, an implant that provides an anastomotic connection, ventricular assist implant, a prosthetic heart valve implant, an inferior vena cava filter implant, a peritoneal dialysis catheter implant, a central nervous system shunt, an intraocular lens, an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 5 OF 59 USPATFULL on STN 2005:241661 USPATFULL ΑN ΤI Electrical devices and anti-scarring agents ΙN Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA PΑ Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PΙ US 20050209666 A1 20050922 ΑI US 2004-6885 A1 20041207 (11) Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING RLI Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004, PENDING 20040709 (60) PRAI US 2004-586861P US 2004-578471P 20040609 (60) US 2003-526541P 20031203 (60) US 2003-525226P 20031124 (60) US 2003-523908P 20031120 (60) US 2003-524023P 20031120 (60) DT Utility FS APPLICATION LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 112 CLMN Exemplary Claim: 1-630 ECL 32 Drawing Page(s) DRWN LN.CNT 14772 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AB Electrical devices (e.g., cardiac rhythm management and neurostimulation devices) for contact with tissue are used in combination with an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the devices are implanted within an animal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 59 USPATFULL on STN

AN 2005:241660 USPATFULL

TI Electrical devices and anti-scarring agents

```
Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050209665
                           A1 20050922
ΑI
       US 2004-998351
                           A1 20041126 (10)
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov
       2004, PENDING
       US 2004-586861P
                           20040709 (60)
PRAI
       US 2004-578471P
                           20040609 (60)
                           20031203 (60)
       US 2003-526541P
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 112
ECL
       Exemplary Claim: 1-11691
DRWN
       32 Drawing Page(s)
LN.CNT 14777
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
AB
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
L12 ANSWER 7 OF 59 USPATFULL on STN
ΑN
       2005:241659 USPATFULL
ΤI
       Electrical devices and anti-scarring agents
ΤN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050209664
                           A1 20050922
ΑI
       US 2004-998349
                           A1 20041126 (10)
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586471P
                           20040709 (60)
       US 2004-578471P
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       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
ECL
       Exemplary Claim: 1-1377
       32 Drawing Page(s)
DRWN
LN.CNT 14786
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
AB
```

devices) for contact with tissue are used in combination with an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the devices are implanted within an animal.

```
L12 ANSWER 8 OF 59 USPATFULL on STN
ΑN
       2005:240095 USPATFULL
ΤI
       Polymer compositions and methods for their use
ΙN
       Hunter, William L., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Takacs-Cox, Aniko, North Vancouver, CANADA
       Avelar, Rui, Vancouver, CANADA
       Loss, Troy A. E., North Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
                          A1 20050922
       US 20050208095
ΑI
       US 2004-996354
                           A1 20041122 (10)
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
RLT
       PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-566569P
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       US 2003-526541P
                           20031203 (60)
                           20031124 (60)
       US 2003-525226P
                           20031120 (60)
       US 2003-523908P
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 101
CLMN
       Exemplary Claim: 1
ECL
       32 Drawing Page(s)
DRWN
LN.CNT 34089
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Compositions comprising anti-fibrotic agent(s) and/or polymeric
       compositions can be used in various medical applications including the
       prevention of surgical adhesions, treatment of inflammatory arthritis,
       treatment of scars and keloids, the treatment of vascular disease, and
       the prevention of cartilage loss.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 9 OF 59 USPATFULL on STN
       2005:234693 USPATFULL
ΑN
ΤI
       Soft tissue implants and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
ΙN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050203635
                           A1 20050915
ΑI
       US 2004-6909
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
RLT
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
                           20040609 (60)
       US 2004-578471P
       US 2003-526541P
                           20031203 (60)
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US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
                           20031120 (60)
       US 2003-524023P
       Utility
DT
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 76
ECL
       Exemplary Claim: 1-3038
       32 Drawing Page(s)
LN.CNT 12596
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 10 OF 59 USPATFULL on STN
ΑN
       2005:226572 USPATFULL
ΤI
       Polymer compositions and methods for their use
       Hunter, William L., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA
ΙN
       Gravett, David M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Takacs-Cox, Aniko, North Vancouver, CANADA
       Avelar, Rui, Vancouver, CANADA
       Loss, Troy A E., North Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
                           A1 20050908
PΙ
       US 20050196421
       US 2004-1417
                           A1 20041201 (11)
ΑI
       Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING
                           20040917 (60)
PRAI
       US 2004-611077P
       US 2004-586861P
                           20040709 (60)
       US 2004-566569P
                           20040428 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 100
CLMN
ECL
       Exemplary Claim: 1-7300
       32 Drawing Page(s)
DRWN
LN.CNT 34222
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Compositions comprising anti-fibrotic agent(s) and/or polymeric
       compositions can be used in various medical applications including the
       prevention of surgical adhesions, treatment of inflammatory arthritis,
       treatment of scars and keloids, the treatment of vascular disease, and
       the prevention of cartilage loss.
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 59 USPATFULL on STN AN 2005:221910 USPATFULL

```
Electrical devices and anti-scarring agents
ΤI
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050192647
                           A1 20050901
ΑI
       US 2004-6898
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
                           20040609 (60)
       US 2004-578471P
                           20031203 (60)
       US 2003-526541P
       US 2003-525226P
                           20031124 (60)
                           20031120 (60)
       US 2003-523908P
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
ECL
       Exemplary Claim: 1-1992
DRWN
       32 Drawing Page(s)
LN.CNT 14794
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
L12 ANSWER 12 OF 59 USPATFULL on STN
       2005:220596 USPATFULL
AN
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050191331
                           A1 20050901
       US 2004-1419
                           A1 20041130 (11)
ΑI
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
RLI
PRAI
       US 2003-518785P
                           20031110 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-526541P
                           20031203 (60)
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
DT
       Utility
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 178
CLMN
       Exemplary Claim: 1-2104
ECL
       28 Drawing Page(s)
DRWN
LN.CNT 56419
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Implants are used in combination with an anti-scarring agent in order to inhibit scarring that may otherwise occur when the implant is placed within an animal. The agent may be any suitable anti-scarring agent, e.g., a cell cycle inhibitor, and may be used in conjunction with a second pharmaceutical agent, e.g., an antibiotic. Suitable implants include intravascular implants, a vascular graft or wrap implant, an implant for hemodialysis access, an implant that provides an anastomotic connection, ventricular assist implant, a prosthetic heart valve implant, an inferior vena cava filter implant, a peritoneal dialysis catheter implant, a central nervous system shunt, an intraocular lens, an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L12 ANSWER 13 OF 59 USPATFULL on STN
ΑN
       2005:215962 USPATFULL
ΤI
       Soft tissue implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
PA
       corporation)
       US 20050187639
                           A1 20050825
РΤ
                           A1 20041207 (11)
ΑI
       US 2004-6892
       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
       US 2004-586861P
                           20040709 (60)
PRAI
                           20040609 (60)
       US 2004-578471P
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 101
CLMN
ECL
       Exemplary Claim: 1-3470
       32 Drawing Page(s)
DRWN
LN.CNT 12657
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
AΒ
       nasal implants) are used in combination with an anti-scarring agent in
```

order to inhibit scarring that may otherwise occur when the implant is

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

placed within an animal.

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L12 ANSWER 14 OF 59 USPATFULL on STN

AN 2005:215923 USPATFULL

TI Electrical devices and anti-scarring agents
IN Hunter, William L., Vancouver, CANADA
Gravett, David M., Vancouver, CANADA
Toleikis, Philip M., Vancouver, CANADA
Maiti, Arpita, Vancouver, CANADA
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Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
PA
       corporation)
РΤ
       US 20050187600
                           A1 20050825
       US 2004-998350
                           A1 20041126 (10)
ΑI
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
       Exemplary Claim: 1-3352
ECL
DRWN
       32 Drawing Page(s)
LN.CNT 14781
AΒ
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
L12 ANSWER 15 OF 59 USPATFULL on STN
       2005:215464 USPATFULL
ΑN
ΤI
       Polymer compositions and methods for their use
       Hunter, William L., Vancouver, CANADA
ΤN
       Toleikis, Philip M., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Takacs-Cox, Aniko, North Vancouver, CANADA
       Avelar, Rui, Vancouver, CANADA
       Loss, Troy A. E., North Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050187140
                           A1 20050825
ΑI
       US 2004-408
                           A1 20041129 (11)
RI.T
       Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
                           20040428 (60)
       US 2004-566569P
       US 2004-611077P
                           20040917 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 103
CLMN
ECL
       Exemplary Claim: 1-5846
       32 Drawing Page(s)
DRWN
LN.CNT 34103
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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Compositions comprising anti-fibrotic agent(s) and/or polymeric AR compositions can be used in various medical applications including the prevention of surgical adhesions, treatment of inflammatory arthritis, treatment of scars and keloids, the treatment of vascular disease, and the prevention of cartilage loss. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 16 OF 59 USPATFULL on STN 2005:214574 USPATFULL ΤI Soft tissue implants and anti-scarring agents ΙN Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PAPΙ US 20050186246 A1 20050825 ΑI US 2004-6883 A1 20041207 (11) RLI Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004, PENDING PRAI US 2004-586861P 20040709 (60) US 2004-578471P 20040609 (60) US 2003-526541P 20031203 (60) 20031124 (60) US 2003-525226P 20031120 (60) US 2003-523908P US 2003-524023P 20031120 (60) Utility DT FS APPLICATION LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 101 CLMN ECL Exemplary Claim: 1-2606 DRWN 32 Drawing Page(s) LN.CNT 12658 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and nasal implants) are used in combination with an anti-scarring agent in order to inhibit scarring that may otherwise occur when the implant is placed within an animal. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 17 OF 59 USPATFULL on STN 2005:214573 USPATFULL ΑN ΤI Implantable sensors and implantable pumps and anti-scarring agents Hunter, William L., Vancouver, CANADA ΙN Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PAPΙ US 20050186245 A1 20050825 ΑI US 2004-6880 20041207 (11) Α1 Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING RLT Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004, PENDING

20040709 (60) 20040609 (60)

20031203 (60)

PRAI

US 2004-586861P

US 2004-578471P US 2003-526541P

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US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
                           20031120 (60)
       US 2003-524023P
       Utility
DT
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 112
ECL
       Exemplary Claim: 1-2785
       32 Drawing Page(s)
LN.CNT 15059
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 18 OF 59 USPATFULL on STN
ΑN
       2005:214572 USPATFULL
ΤI
       Polymer compositions and methods for their use
       Hunter, William L., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA
ΙN
       Gravett, David M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Takacs-Cox, Aniko, North Vancouver, CANADA
       Avelar, Rui, Vancouver, CANADA
       Loss, Troy A. E., North Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050186244
                           A1 20050825
       US 2004-1790
                           A1 20041202 (11)
ΑI
       Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING
                           20040917 (60)
PRAI
       US 2004-611077P
       US 2004-586861P
                           20040709 (60)
       US 2004-566569P
                           20040428 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 103
CLMN
ECL
       Exemplary Claim: 1-8540
       32 Drawing Page(s)
DRWN
LN.CNT 34060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Compositions comprising anti-fibrotic agent(s) and/or polymeric
       compositions can be used in various medical applications including the
       prevention of surgical adhesions, treatment of inflammatory arthritis,
       treatment of scars and keloids, the treatment of vascular disease, and
       the prevention of cartilage loss.
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 19 OF 59 USPATFULL on STN 2005:214567 USPATFULL MΑ

```
Implantable sensors and implantable pumps and anti-scarring agents
ΤI
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050186239
                           A1 20050825
ΑI
       US 2004-6897
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
       US 2004-586861P
PRAI
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
                           20031120 (60)
       US 2003-523908P
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
ECL
       Exemplary Claim: 1-3058
DRWN
       32 Drawing Page(s)
LN.CNT 15050
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 20 OF 59 USPATFULL on STN
ΑN
       2005:212068 USPATFULL
ΤI
       Polymer compositions and methods for their use
       Hunter, William L., Vancouver, CANADA
IN
       Toleikis, Philip M., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Takacs-Cox, Aniko, North Vancouver, CANADA
       Avelar, Rui, Vancouver, CANADA
       Loss, Troy A.E., North Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050183731
                           A1 20050825
       US 2004-6908
                           A1
                               20041207 (11)
ΑI
       Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING
       US 2004-611077P
PRAI
                           20040917 (60)
       US 2004-586861P
                           20040709 (60)
       US 2004-566569P
                           20040428 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       Utility
DT
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
```

CLMN Number of Claims: 52 ECL Exemplary Claim: 1-8061 DRWN 32 Drawing Page(s)

LN.CNT 34032

AB Compositions comprising anti-fibrotic agent(s) and/or polymeric compositions can be used in various medical applications including the prevention of surgical adhesions, treatment of inflammatory arthritis, treatment of scars and keloids, the treatment of vascular disease, and the prevention of cartilage loss.

```
L12 ANSWER 21 OF 59 USPATFULL on STN
ΑN
       2005:212065 USPATFULL
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
       corporation)
       US 20050183728
                               20050825
PΙ
                           A1
                           A1 20041207 (11)
ΑI
       US 2004-7836
RLI
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
       US 2003-518785P
                           20031110 (60)
PRAI
                           20031120 (60)
       US 2003-523908P
       US 2003-524023P
                           20031120 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-526541P
                           20031203 (60)
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 178
ECL
       Exemplary Claim: 1-3411
DRWN
       28 Drawing Page(s)
LN.CNT 56413
       Implants are used in combination with an anti-scarring agent in order to
AΒ
```

Implants are used in combination with an anti-scarring agent in order to inhibit scarring that may otherwise occur when the implant is placed within an animal. The agent may be any suitable anti-scarring agent, e.g., a cell cycle inhibitor, and may be used in conjunction with a second pharmaceutical agent, e.g., an antibiotic. Suitable implants include intravascular implants, a vascular graft or wrap implant, an implant for hemodialysis access, an implant that provides an anastomotic connection, ventricular assist implant, a prosthetic heart valve implant, an inferior vena cava filter implant, a peritoneal dialysis catheter implant, a central nervous system shunt, an intraocular lens, an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant.

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L12 ANSWER 22 OF 59 USPATFULL on STN
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AN 2005:210011 USPATFULL

TI Soft tissue implants and anti-scarring agents

IN Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA

```
Maiti, Arpita, Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
       US 20050182496
РΤ
                           A1 20050818
       US 2004-6906
                           A1 20041207 (11)
ΑI
       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
RLT
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 76
CLMN
       Exemplary Claim: 1-3902
ECL
DRWN
       32 Drawing Page(s)
LN.CNT 12588
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 23 OF 59 USPATFULL on STN
       2005:209984 USPATFULL
ΑN
ΤТ
       Electrical devices and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
PA
       corporation)
PΙ
       US 20050182469
                           A1 20050818
ΑI
       US 2004-7837
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 120
CLMN
ECL
       Exemplary Claim: 1-2803
       32 Drawing Page(s)
DRWN
LN.CNT 14838
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
```

devices) for contact with tissue are used in combination with an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the devices are implanted within an animal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 24 OF 59 USPATFULL on STN 2005:209983 USPATFULL ΤI Electrical devices and anti-scarring agents ΙN Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA PΑ Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PΙ US 20050182468 A1 20050818 US 2004-6891 ΑI A1 20041207 (11) Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING RLT Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004, PENDING PRAI US 2004-586861P 20040709 (60) US 2004-578471P 20040609 (60) US 2003-526541P 20031203 (60) US 2003-525226P 20031124 (60) 20031120 (60) US 2003-523908P 20031120 (60) US 2003-524023P DT Utility FS APPLICATION LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 112 CLMN Exemplary Claim: 1-1720 ECL 32 Drawing Page(s) DRWN LN.CNT 14768 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Electrical devices (e.g., cardiac rhythm management and neurostimulation devices) for contact with tissue are used in combination with an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the devices are implanted within an animal. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 25 OF 59 USPATFULL on STN 2005:209982 USPATFULL ΑN ΤI Electrical devices and anti-scarring agents ΙN Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PAPΙ US 20050182467 A1 20050818 ΑI US 2004-6884 A1 20041207 (11) Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING RLT Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004, PENDING

> 20040709 (60) 20040609 (60)

20031203 (60)

PRAI

US 2004-586861P

US 2004-578471P US 2003-526541P

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US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
       Utility
DT
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 112
ECL
       Exemplary Claim: 1-1168
       32 Drawing Page(s)
LN.CNT 14785
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 26 OF 59 USPATFULL on STN
ΑN
       2005:209978 USPATFULL
ΤI
       Polymer compositions and methods for their use
       Hunter, William L., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA
ΙN
       Gravett, David M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Takacs-Cox, Aniko, North Vancouver, CANADA
       Avelar, Rui, Vancouver, CANADA
       Loss, Troy A. E., North Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
PA
       corporation)
       US 20050182463
                           A1 20050818
PΙ
       US 2004-1788
                           A1 20041202 (11)
ΑI
RLT
       Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING
PRAI
       US 2004-611077P
                           20040917 (60)
       US 2004-586861P
                           20040709 (60)
       US 2004-566569P
                           20040428 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
                           20031120 (60)
       US 2003-523908P
       Utility
DΤ
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 125
CLMN
ECL
       Exemplary Claim: 1-8059
DRWN
       32 Drawing Page(s)
LN.CNT 34070
AΒ
       Compositions comprising anti-fibrotic agent(s) and/or polymeric
       compositions can be used in various medical applications including the
       prevention of surgical adhesions, treatment of inflammatory arthritis,
       treatment of scars and keloids, the treatment of vascular disease, and
       the prevention of cartilage loss.
```

L12 ANSWER 27 OF 59 USPATFULL on STN AN 2005:209965 USPATFULL

```
Electrical devices and anti-scarring agents
ΤI
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050182450
                           A1 20050818
ΑI
       US 2004-6890
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996355, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
                           20031120 (60)
       US 2003-523908P
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
       Exemplary Claim: 1-349
ECL
DRWN
       32 Drawing Page(s)
LN.CNT 14792
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
L12 ANSWER 28 OF 59 USPATFULL on STN
       2005:209494 USPATFULL
ΑN
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050181977
                          A1 20050818
       US 2004-986231
ΑI
                           A1 20041110 (10)
       US 2003-518785P
                           20031110 (60)
PRAI
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-526541P
                           20031203 (60)
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 182
CLMN
ECL
       Exemplary Claim: 1
       28 Drawing Page(s)
DRWN
LN.CNT 56396
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

Implants are used in combination with an anti-scarring agent in order to inhibit scarring that may otherwise occur when the implant is placed within an animal. The agent may be any suitable anti-scarring agent, e.g., a cell cycle inhibitor, and may be used in conjunction with a second pharmaceutical agent, e.g., an antibiotic. Suitable implants include intravascular implants, a vascular graft or wrap implant, an implant for hemodialysis access, an implant that provides an anastomotic connection, ventricular assist implant, a prosthetic heart valve implant, an inferior vena cava filter implant, a peritoneal dialysis catheter implant, a central nervous system shunt, an intraocular lens, an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L12 ANSWER 29 OF 59 USPATFULL on STN
ΑN
       2005:208533 USPATFULL
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΑ
                          A1 20050818
PΙ
       US 20050181011
ΑI
       US 2004-1792
                          A1 20041202 (11)
RLI
      Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
PRAI
      US 2003-518785P 20031110 (60)
       US 2003-523908P
                          20031120 (60)
       US 2003-524023P
                          20031120 (60)
       US 2003-525226P
                          20031124 (60)
       US 2003-526541P
                          20031203 (60)
       US 2004-586861P
                          20040709 (60)
       US 2004-578471P
                          20040609 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
      Number of Claims: 177
CLMN
ECL
       Exemplary Claim: 1-4994
       28 Drawing Page(s)
LN.CNT 56421
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Implants are used in combination with an anti-scarring agent in order to
       inhibit scarring that may otherwise occur when the implant is placed
       within an animal. The agent may be any suitable anti-scarring agent,
       e.g., a cell cycle inhibitor, and may be used in conjunction with a
       second pharmaceutical agent, e.g., an antibiotic. Suitable implants
       include intravascular implants, a vascular graft or wrap implant, an
       implant for hemodialysis access, an implant that provides an anastomotic
       connection, ventricular assist implant, a prosthetic heart valve
       implant, an inferior vena cava filter implant, a peritoneal dialysis
       catheter implant, a central nervous system shunt, an intraocular lens,
       an implant for glaucoma drainage, a penile implant, an endotracheal
       tube, a tracheostomy tube, a gastrointestinal device, and a spinal
       implant.
```

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L12 ANSWER 30 OF 59 USPATFULL on STN
       2005:208532 USPATFULL
ΑN
ΤТ
       Implantable sensors and implantable pumps and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
ΙN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050181010
                           A1 20050818
ΑI
       US 2004-1789
                           A1 20041201 (11)
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLT
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
                           20031203 (60)
       US 2003-526541P
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 109
CLMN
ECL
       Exemplary Claim: 1-296
       32 Drawing Page(s)
DRWN
LN.CNT 15014
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Pumps and sensors for contact with tissue are used in combination with
AB
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 31 OF 59 USPATFULL on STN
ΑN
       2005:208531 USPATFULL
ΤI
       Implantable sensors and implantable pumps and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
                           A1 20050818
РΤ
       US 20050181009
       US 2004-1787
ΑI
                               20041201 (11)
                           A1
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
                           20031124 (60)
       US 2003-525226P
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 110
CLMN
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Exemplary Claim: 1-570 32 Drawing Page(s) DRWN LN.CNT 15035 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Pumps and sensors for contact with tissue are used in combination with an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the pumps and sensors are implanted within an animal. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 32 OF 59 USPATFULL on STN ΑN 2005:208530 USPATFULL ΤI Medical implants and anti-scarring agents ΙN Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Signore, Pierre E., Vancouver, CANADA Liggins, Richard T., Coquitlam, CANADA PAAngiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PΙ US 20050181008 A1 20050818 A1 20041202 (11) ΑI US 2004-1786 Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING RLI PRAI US 2003-518785P 20031110 (60) US 2003-523908P 20031120 (60) US 2003-524023P 20031120 (60) 20031124 (60) US 2003-525226P US 2003-526541P 20031203 (60) US 2004-586861P 20040709 (60) US 2004-578471P 20040609 (60) DT Utility APPLICATION FS SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE LREP 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 178 CLMN ECL Exemplary Claim: 1-4736 DRWN 28 Drawing Page(s) LN.CNT 56377 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Implants are used in combination with an anti-scarring agent in order to AΒ inhibit scarring that may otherwise occur when the implant is placed within an animal. The agent may be any suitable anti-scarring agent, e.g., a cell cycle inhibitor, and may be used in conjunction with a second pharmaceutical agent, e.g., an antibiotic. Suitable implants include intravascular implants, a vascular graft or wrap implant, an implant for hemodialysis access, an implant that provides an anastomotic connection, ventricular assist implant, a prosthetic heart valve implant, an inferior vena cava filter implant, a peritoneal dialysis catheter implant, a central nervous system shunt, an intraocular lens, an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 33 OF 59 USPATFULL on STN ΑN 2005:208529 USPATFULL

Soft tissue implants and anti-scarring agents

Hunter, William L., Vancouver, CANADA Gravett, David M., Vancouver, CANADA

ECT.

ΤI

ΙN

```
Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050181007
                           A1 20050818
                           A1 20041130 (11)
ΑI
       US 2004-1415
       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
       US 2004-586861P
                           20040709 (60)
PRAI
       US 2004-578471P
                           20040609 (60)
                           20031203 (60)
       US 2003-526541P
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 126
CLMN
ECL
       Exemplary Claim: 1-444
DRWN
       32 Drawing Page(s)
LN.CNT 12675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 34 OF 59 USPATFULL on STN
       2005:208527 USPATFULL
ΑN
ΤI
       Implantable sensors and implantable pumps and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
PA
       corporation)
PΙ
       US 20050181005
                           A1 20050818
ΑI
       US 2004-6901
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
ECL
       Exemplary Claim: 1-2510
       32 Drawing Page(s)
DRWN
LN.CNT 15035
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

Pumps and sensors for contact with tissue are used in combination with AR an anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit scarring that may otherwise occur when the pumps and sensors are implanted within an animal. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 35 OF 59 USPATFULL on STN ΑN 2005:205930 USPATFULL ΤI Polymer compositions and methods for their use ΙN Hunter, William L., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Liggins, Richard T., Coquitlam, CANADA Takacs-Cox, Aniko, North Vancouver, CANADA Avelar, Rui, Vancouver, CANADA Loss, Troy A. E., North Vancouver, CANADA Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PAPΙ US 20050178396 A1 20050818 ΑI US 2004-6905 A1 20041207 (11) RLI Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING US 2004-611077P 20040917 (60) PRAI 20040709 (60) US 2004-586861P 20040428 (60) US 2004-566569P US 2003-526541P 20031203 (60) US 2003-525226P 20031124 (60) US 2003-523908P 20031120 (60) DT Utility FS APPLICATION LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 50 CLMN ECL Exemplary Claim: 1-8063 DRWN 32 Drawing Page(s) LN.CNT 33965 Compositions comprising anti-fibrotic agent(s) and/or polymeric AB compositions can be used in various medical applications including the prevention of surgical adhesions, treatment of inflammatory arthritis, treatment of scars and keloids, the treatment of vascular disease, and the prevention of cartilage loss. L12 ANSWER 36 OF 59 USPATFULL on STN 2005:205929 USPATFULL ΑN ΤI Polymer compositions and methods for their use Hunter, William L., Vancouver, CANADA TNToleikis, Philip M., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Liggins, Richard T., Coquitlam, CANADA Takacs-Cox, Aniko, North Vancouver, CANADA Avelar, Rui, Vancouver, CANADA Loss, Troy A. E., North Vancouver, CANADA PAAngiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)

A1 20050818

A1 20041207 (11)

Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING

Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,

PΙ

ΑI

RLT

US 20050178395

US 2004-6900

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PENDING
PRAT
       US 2004-611077P
                           20040917 (60)
                           20040709 (60)
       US 2004-586861P
       US 2004-566569P
                          20040428 (60)
       US 2003-526541P
                          20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                          20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 58
ECL
       Exemplary Claim: 1-7302
DRWN
       32 Drawing Page(s)
LN.CNT 34043
       Compositions comprising anti-fibrotic agent(s) and/or polymeric
AR
       compositions can be used in various medical applications including the
       prevention of surgical adhesions, treatment of inflammatory arthritis,
       treatment of scars and keloids, the treatment of vascular disease, and
       the prevention of cartilage loss.
L12 ANSWER 37 OF 59 USPATFULL on STN
ΑN
       2005:203799 USPATFULL
TΙ
       Medical implants and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
ΤN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Angiotech International AG, Zug, SWITZERLAND, CH (non-U.S. corporation)
PA
                           A1 20050811
PΙ
       US 20050177225
       US 2004-6895
                           A1 20041207 (11)
AΙ
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
RLI
PRAI
       US 2004-586861P
                          20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                          20031203 (60)
       US 2003-525226P
                          20031124 (60)
       US 2003-523908P
                          20031120 (60)
       US 2003-524023P
                          20031120 (60)
       US 2003-518785P
                          20031110 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 173
CLMN
ECL
       Exemplary Claim: 1-11788
       28 Drawing Page(s)
DRWN
LN.CNT 56371
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Implants are used in combination with an anti-scarring agent in order to
       inhibit scarring that may otherwise occur when the implant is placed
       within an animal. The agent may be any suitable anti-scarring agent,
       e.g., a cell cycle inhibitor, and may be used in conjunction with a
       second pharmaceutical agent, e.g., an antibiotic. Suitable implants
       include intravascular implants, a vascular graft or wrap implant, an
       implant for hemodialysis access, an implant that provides an anastomotic
       connection, ventricular assist implant, a prosthetic heart valve
       implant, an inferior vena cava filter implant, a peritoneal dialysis
       catheter implant, a central nervous system shunt, an intraocular lens,
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an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 38 OF 59 USPATFULL on STN ΑN 2005:202285 USPATFULL ΤI Polymer compositions and methods for their use ΙN Hunter, William L., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Liggins, Richard T., Coquitlam, CANADA Takacs-Cox, Aniko, North Vancouver, CANADA Avelar, Rui, Vancouver, CANADA Loss, Troy A.E., North Vancouver, CANADA PΑ Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PΙ A1 20050811 US 20050175703 ΑI US 2004-6888 A1 20041207 (11) Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING RLT Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING PRAI US 2004-611077P 20040917 (60) US 2004-586861P 20040709 (60) 20040428 (60) US 2004-566569P 20031203 (60) US 2003-526541P US 2003-525226P 20031124 (60) US 2003-523908P 20031120 (60) DT Utility FS APPLICATION SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE LREP 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 55 CLMN ECL Exemplary Claim: 1-7576 DRWN 32 Drawing Page(s) LN.CNT 33992 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Compositions comprising anti-fibrotic agent(s) and/or polymeric compositions can be used in various medical applications including the prevention of surgical adhesions, treatment of inflammatory arthritis, treatment of scars and keloids, the treatment of vascular disease, and the prevention of cartilage loss. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L12 ANSWER 39 OF 59 USPATFULL on STN 2005:202247 USPATFULL ΑN ΤТ Polymer compositions and methods for their use Hunter, William L., Vancouver, CANADA ΙN Toleikis, Philip M., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Liggins, Richard T., Coquitlam, CANADA Takacs-Cox, Aniko, North Vancouver, CANADA Avelar, Rui, Vancouver, CANADA Loss, Troy A. E., North Vancouver, CANADA PΑ Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PΙ US 20050175665 A1 20050811 A1 20041207 (11) ΑТ US 2004-6896

Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING

RLI

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Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
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                           20040917 (60)
PRAT
       US 2004-611077P
       US 2004-586861P
                           20040709 (60)
       US 2004-566569P
                           20040428 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 51
CLMN
ECL
       Exemplary Claim: 1-7822
DRWN
       32 Drawing Page(s)
LN.CNT 33978
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Compositions comprising anti-fibrotic agent(s) and/or polymeric
AB
       compositions can be used in various medical applications including the
       prevention of surgical adhesions, treatment of inflammatory arthritis,
       treatment of scars and keloids, the treatment of vascular disease, and
       the prevention of cartilage loss.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 40 OF 59 USPATFULL on STN
       2005:202246 USPATFULL
ΑN
ΤI
       Implantable sensors and implantable pumps and anti-scarring agents
IN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
                           A1 20050811
       US 20050175664
       US 2004-4672
                           A1 20041202 (11)
ΑI
RLT
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
       US 2004-586861P
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       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
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       US 2003-524023P
                           20031120 (60)
DТ
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 109
ECL
       Exemplary Claim: 1-851
DRWN
       32 Drawing Page(s)
LN.CNT 15038
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L12 ANSWER 41 OF 59 USPATFULL on STN
       2005:202245 USPATFULL
ΑN
ΤТ
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050175663
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ΑI
       US 2004-1791
                           A1 20041202 (11)
RLI
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
PRAI
       US 2003-518785P
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       US 2003-523908P
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       US 2003-524023P
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       US 2003-525226P
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       US 2003-526541P
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       US 2004-578471P
                           20040609 (60)
DT
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FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 180
CLMN
       Exemplary Claim: 1-3944
ECL
       28 Drawing Page(s)
LN.CNT 56451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Implants are used in combination with an anti-scarring agent in order to
       inhibit scarring that may otherwise occur when the implant is placed
       within an animal. The agent may be any suitable anti-scarring agent,
       e.g., a cell cycle inhibitor, and may be used in conjunction with a
       second pharmaceutical agent, e.g., an antibiotic. Suitable implants
       include intravascular implants, a vascular graft or wrap implant, an
       implant for hemodialysis access, an implant that provides an anastomotic
       connection, ventricular assist implant, a prosthetic heart valve
       implant, an inferior vena cava filter implant, a peritoneal dialysis
       catheter implant, a central nervous system shunt, an intraocular lens,
       an implant for glaucoma drainage, a penile implant, an endotracheal
       tube, a tracheostomy tube, a gastrointestinal device, and a spinal
       implant.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 42 OF 59 USPATFULL on STN
       2005:195820 USPATFULL
ΑN
ΤI
       Implantable sensors and implantable pumps and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
                           A1 20050804
A1 20041202 (11)
PΙ
       US 20050169961
ΑI
       US 2004-4675
RLI
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       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
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PRAI
       US 2004-586861P
                           20040609 (60)
       US 2004-578471P
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US 2003-526541P
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 118
       Exemplary Claim: 1-1941
       32 Drawing Page(s)
LN.CNT 15063
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 43 OF 59 USPATFULL on STN
ΑN
       2005:195819 USPATFULL
ΤI
       Implantable sensors and implantable pumps and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND, 6304 (non-U.S.
       corporation)
                           A1 20050804
PΙ
       US 20050169960
ΑI
       US 2004-4671
                           A1 20041202 (11)
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
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       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 110
CLMN
       Exemplary Claim: 1-3328
ECL
       32 Drawing Page(s)
DRWN
LN.CNT 15057
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 44 OF 59 USPATFULL on STN
AN
       2005:190568 USPATFULL
TΙ
       Medical implants and anti-scarring agents
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TM

Hunter, William L., Vancouver, CANADA

```
Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Angiotech International AG, Zug, SWEDEN (non-U.S. corporation)
PA
PΙ
       US 20050165488
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ΑI
       US 2004-6912
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
RLI
PRAI
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       US 2003-526541P
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       US 2003-525226P
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
       US 2003-518785P
                           20031110 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 176
ECL
       Exemplary Claim: 1-3153
DRWN
       28 Drawing Page(s)
LN.CNT 56407
AB
       Implants are used in combination with an anti-scarring agent in order to
       inhibit scarring that may otherwise occur when the implant is placed
       within an animal. The agent may be any suitable anti-scarring agent,
       e.g., a cell cycle inhibitor, and may be used in conjunction with a
       second pharmaceutical agent, e.g., an antibiotic. Suitable implants
       include intravascular implants, a vascular graft or wrap implant, an
       implant for hemodialysis access, an implant that provides an anastomotic
       connection, ventricular assist implant, a prosthetic heart valve
       implant, an inferior vena cava filter implant, a peritoneal dialysis
       catheter implant, a central nervous system shunt, an intraocular lens,
       an implant for glaucoma drainage, a penile implant, an endotracheal
       tube, a tracheostomy tube, a gastrointestinal device, and a spinal
       implant.
L12 ANSWER 45 OF 59 USPATFULL on STN
ΑN
       2005:182973 USPATFULL
ΤI
       Implantable sensors and implantable pumps and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050158356
                           A1 20050721
                           A1 20041122 (10)
ΑI
       US 2004-996352
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
RLI
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
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       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
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                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
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DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
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Number of Claims: 117
CLMN
ECL
       Exemplary Claim: 1
       32 Drawing Page(s)
DRWN
LN.CNT 15058
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 46 OF 59 USPATFULL on STN
ΑN
       2005:178293 USPATFULL
TΙ
       Implantable sensors and implantable pumps and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
TM
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vacouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050154374
                           A1 20050714
                           A1 20041207 (11)
ΑI
       US 2004-6882
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
PRAI
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       US 2003-526541P
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       US 2003-525226P
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 112
       Exemplary Claim: 1-2240
ECL
DRWN
       32 Drawing Page(s)
LN.CNT 15052
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 47 OF 59 USPATFULL on STN
L12
AN
       2005:176868 USPATFULL
ΤI
       Soft tissue implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050152948
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ΑI
       US 2004-7838
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       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
RLT
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Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,

6300, SEATTLE, WA, 98104-7092, US

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PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
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PRAT
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 96
CLMN
ECL
       Exemplary Claim: 1-2174
DRWN
       32 Drawing Page(s)
LN.CNT 12627
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
AΒ
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 48 OF 59 USPATFULL on STN
       2005:176867 USPATFULL
ΑN
ТΤ
       Soft tissue implants and anti-scarring agents
TN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050152947
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       US 2004-6903
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AΙ
       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
RLI
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       2004, PENDING
PRAI
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       US 2003-526541P
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                          20031124 (60)
       US 2003-523908P
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       US 2003-524023P
                          20031120 (60)
       Utility
DΤ
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 96
CLMN
ECL
       Exemplary Claim: 1-1742
DRWN
       32 Drawing Page(s)
LN.CNT 12637
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 49 OF 59 USPATFULL on STN

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2005:176866 USPATFULL
ΑN
       Implantable sensors and implantable pumps and anti-scarring agents
ΤТ
       Hunter, William L., Vancouver, CANADA
TN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050152946
                           A1 20050714
ΑI
       US 2004-6894
                           A1 20041207 (11)
       Continuation of Ser. No. US 2004-996352, filed on 22 Nov 2004, PENDING
RLI
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       2004, PENDING
                           20040709 (60)
PRAI
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                           20040609 (60)
       US 2004-578471P
       US 2003-526541P
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 112
CLMN
       Exemplary Claim: 1-1126
ECL
       32 Drawing Page(s)
DRWN
LN.CNT 15056
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Pumps and sensors for contact with tissue are used in combination with
       an anti-scarring agent (e.g., a cell cycle inhibitor) in order to
       inhibit scarring that may otherwise occur when the pumps and sensors are
       implanted within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 50 OF 59 USPATFULL on STN
ΑN
       2005:176865 USPATFULL
ΤI
       Soft tissue implants and anti-scarring agents
       Hunter, William L., Vancouver, CANADA
ΤN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
PA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
                           A1 20050714
PΙ
       US 20050152945
       US 2004-6887
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ΑI
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RLI
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       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
       US 2004-586861P
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PRAI
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
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       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
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       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 96
CLMN
ECL
       Exemplary Claim: 1-1310
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LN.CNT 12592
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 51 OF 59 USPATFULL on STN
       2005:176864 USPATFULL
TΙ
       Soft tissue implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
                           A1 20050714
       US 20050152944
ΑI
       US 2004-6881
                           A1 20041207 (11)
RLT
       Continuation of Ser. No. US 2004-996353, filed on 22 Nov 2004, PENDING
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
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       2004, PENDING
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PRAI
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       US 2003-524023P
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DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 96
CLMN
ECL
       Exemplary Claim: 1-878
DRWN
       32 Drawing Page(s)
LN.CNT 12628
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 52 OF 59 USPATFULL on STN
       2005:176861 USPATFULL
ΑN
       Soft tissue implants and anti-scarring agents
ΤТ
       Hunter, William L., Vancouver, CANADA
ΙN
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
                           A1 20050714
A1 20041122 (10)
PΙ
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ΑI
       US 2004-996353
RLI
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
                           20040709 (60)
PRAI
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                           20040609 (60)
       US 2004-578471P
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32 Drawing Page(s)

DRWN

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US 2003-526541P
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       US 2003-525226P
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       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
       Number of Claims: 132
       Exemplary Claim: 1
DRWN
       32 Drawing Page(s)
LN.CNT 12685
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and
       nasal implants) are used in combination with an anti-scarring agent in
       order to inhibit scarring that may otherwise occur when the implant is
       placed within an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 53 OF 59 USPATFULL on STN
ΑN
       2005:172409 USPATFULL
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
      Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
PΑ
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΙ
       US 20050149158
                          A1 20050707
       US 2004-409
                           A1 20041129 (11)
ΑI
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
RLI
PRAI
      US 2003-518785P
                       20031110 (60)
      US 2003-523908P
                          20031120 (60)
       US 2003-524023P
                          20031120 (60)
       US 2003-525226P
                          20031124 (60)
       US 2003-526541P
                          20031203 (60)
       US 2004-586861P
                          20040709 (60)
       US 2004-578471P
                          20040609 (60)
DT
       Utility
FS
      APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
       6300, SEATTLE, WA, 98104-7092, US
      Number of Claims: 178
CLMN
       Exemplary Claim: 1-274
ECL
DRWN
       28 Drawing Page(s)
LN.CNT 56404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Implants are used in combination with an anti-scarring agent in order to
AB
       inhibit scarring that may otherwise occur when the implant is placed
       within an animal. The agent may be any suitable anti-scarring agent,
       e.g., a cell cycle inhibitor, and may be used in conjunction with a
       second pharmaceutical agent, e.g., an antibiotic. Suitable implants
       include intravascular implants, a vascular graft or wrap implant, an
       implant for hemodialysis access, an implant that provides an anastomotic
       connection, ventricular assist implant, a prosthetic heart valve
       implant, an inferior vena cava filter implant, a peritoneal dialysis
       catheter implant, a central nervous system shunt, an intraocular lens,
       an implant for glaucoma drainage, a penile implant, an endotracheal
       tube, a tracheostomy tube, a gastrointestinal device, and a spinal
```

implant.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L12 ANSWER 54 OF 59 USPATFULL on STN
       2005:172408 USPATFULL
ΑN
TΙ
       Electrical devices and anti-scarring agents
ΤN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050149157
                           A1 20050707
ΑI
       US 2004-996355
                           A1 20041122 (10)
       Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004,
RLI
       PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov
       2004, PENDING
                           20040709 (60)
PRAI
       US 2004-586861P
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                           20031120 (60)
DT
       Utility
FS
       APPLICATION
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE
LREP
       6300, SEATTLE, WA, 98104-7092, US
CLMN
       Number of Claims: 111
ECL
       Exemplary Claim: 1
DRWN
       32 Drawing Page(s)
LN.CNT 14769
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Electrical devices (e.g., cardiac rhythm management and neurostimulation
       devices) for contact with tissue are used in combination with an
       anti-scarring agent (e.g., a cell cycle inhibitor) in order to inhibit
       scarring that may otherwise occur when the devices are implanted within
       an animal.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 55 OF 59 USPATFULL on STN
ΑN
       2005:172331 USPATFULL
ΤI
       Medical implants and anti-scarring agents
ΙN
       Hunter, William L., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Toleikis, Philip M., Vancouver, CANADA
       Maiti, Arpita, Vancouver, CANADA
       Signore, Pierre E., Vancouver, CANADA
       Liggins, Richard T., Coquitlam, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PA
PΙ
       US 20050149080
                           A1 20050707
                           A1 20041130 (11)
       US 2004-1418
ΑI
       Continuation of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING
RLI
PRAI
       US 2004-586861P
                           20040709 (60)
       US 2004-578471P
                           20040609 (60)
       US 2003-526541P
                           20031203 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-523908P
                           20031120 (60)
       US 2003-524023P
                          20031120 (60)
       US 2003-518785P
                          20031110 (60)
DT
       Utility
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APPLICATION FS SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE LREP 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 178 CLMN Exemplary Claim: 1-806 ECL 28 Drawing Page(s) DRWN LN.CNT 56418 Implants are used in combination with an anti-scarring agent in order to AΒ inhibit scarring that may otherwise occur when the implant is placed within an animal. The agent may be any suitable anti-scarring agent, e.g., a cell cycle inhibitor, and may be used in conjunction with a second pharmaceutical agent, e.g., an antibiotic. Suitable implants include intravascular implants, a vascular graft or wrap implant, an implant for hemodialysis access, an implant that provides an anastomotic connection, ventricular assist implant, a prosthetic heart valve implant, an inferior vena cava filter implant, a peritoneal dialysis catheter implant, a central nervous system shunt, an intraocular lens, an implant for glaucoma drainage, a penile implant, an endotracheal tube, a tracheostomy tube, a gastrointestinal device, and a spinal implant. L12 ANSWER 56 OF 59 USPATFULL on STN 2005:164738 USPATFULL ΑN TΙ Soft tissue implants and anti-scarring agents Hunter, William L., Vancouver, CANADA ΤN Gravett, David M., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA PΑ Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation) PΙ US 20050142162 A1 20050630 A1 20041201 (11) ΑI US 2004-1416 RLI Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986230, filed on 10 Nov 2004, PENDING 20040709 (60) PRAI US 2004-586861P US 2004-578471P 20040609 (60) US 2003-526541P 20031203 (60) US 2003-524023P 20031120 (60) US 2003-523908P 20031120 (60) US 2003-525226P 20031124 (60) DT Utility FS APPLICATION LREP SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US Number of Claims: 117 CLMN Exemplary Claim: 1-4334 ECL 32 Drawing Page(s) DRWN LN.CNT 12679 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AB Soft tissue implants (e.g., breast, pectoral, chin, facial, lip, and nasal implants) are used in combination with an anti-scarring agent in order to inhibit scarring that may otherwise occur when the implant is

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 57 OF 59 USPATFULL on STN

placed within an animal.

AN 2004:328492 USPATFULL

TI Anastomotic connector devices

IN Hunter, William L., Vancouver, CANADA

```
Toleikis, Philip M., Vancouver, CANADA
       Gravett, David M., Vancouver, CANADA
       Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)
PΑ
PΙ
       US 20040260318
                           A1 20041223
ΑТ
       US 2004-853023
                           A1 20040524 (10)
       US 2003-473185P
                           20030523 (60)
PRAI
       US 2003-523908P
                           20031120 (60)
       US 2003-525226P
                           20031124 (60)
       US 2003-526541P
                           20031203 (60)
DT
       Utility
FS
       APPLICATION
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300,
       SEATTLE, WA, 98104-7092
CLMN
       Number of Claims: 117
ECL
       Exemplary Claim: 1
DRWN
       19 Drawing Page(s)
LN.CNT 6906
       Anastomotic connector devices are provided which release a therapeutic
AB
       agent. The therapeutic agent may be an anti-scarring agent that inhibits
       stenosis caused by the presence of the anastomotic connector device.
L12 ANSWER 58 OF 59 USPATFULL on STN
ΑN
       2004:274400 USPATFULL
TΙ
       Small molecule antagonists of BCL-2 family proteins
       Wang, Shaomeng, Saline, MI, UNITED STATES
ΤN
       Yang, Dajun, Rockville, MD, UNITED STATES
PA
       The Regents of the University of Michigan, Ann Arbor, MI (U.S.
       corporation)
       Georgetown University, Washington, DC (U.S. corporation)
                           A1 20041028
PΙ
       US 20040214902
       US 2003-729156
                           A1 20031205 (10)
AΙ
       Continuation-in-part of Ser. No. US 2002-158769, filed on 30 May 2002,
RLT
       ABANDONED Continuation-in-part of Ser. No. WO 2002-US17206, filed on 30
       May 2002, PENDING
       US 2001-293983P
PRAI
                           20010530 (60)
DT
       Utility
       APPLICATION
FS
       David A. Casimir, MEDLEN & CARROLL, LLP, Suite 350, 101 Howard Street,
LREP
       San Francisco, CA, 94105
       Number of Claims: 51
CLMN
ECL
       Exemplary Claim: 1
DRWN
       55 Drawing Page(s)
LN.CNT 8211
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The present invention relates to naturally occurring and chemically
       synthesized small molecule antagonists of Bcl-2 family proteins. In
       particular, the present invention provides gossypol compounds (e.g.,
       isomers, enantiomers, racemic compounds, metabolites, derivatives,
       pharmaceutically acceptable salts, in combination with acids or bases,
       and the like) and methods of using these compounds as antagonists of the
       anti-apoptotic effects of Bcl-2 family member proteins (e.g., Bcl-2,
       Bcl-X.sub.L, and the like). The present invention also provides
       compositions comprising gossypol compounds and optionally one or more
       additional therapeutic agents (e.g., anticancer/chemotherapeutic
       agents). The present invention also provides methods for treating
       diseases and pathologies (e.g., neoplastic diseases) comprising
       administering a composition comprising gossypol compounds and optionally
       one or more additional therapeutic agents (e.g.,
       anticancer/chemotherapeutic agents) and/or techniques (e.g.,
       radiation therapies, surgical interventions, and the like) to a
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subject or in vitro cells, tissues, and organs.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 59 OF 59 USPATFULL on STN ΑN 90:79881 USPATFULL ΤI Stable lyophilized form of (S)-(+)-bis-4,4'-(1-methyl-1,2ethanediyl)2,6-piperazinedione and solutions thereof ΙN Palepu, Nagesh R., Franklin County, OH, United States Martin, Joyce W., Franklin County, OH, United States Erbamont Inc., Dublin, OH, United States (U.S. corporation) PΑ PΙ 19901016 US 4963551 ΑI US 1990-463844 19900112 (7) Continuation of Ser. No. US 1987-136036, filed on 21 Dec 1987, now RLI abandoned DT Utility FS Granted EXNAM Primary Examiner: Bell, Mark L.; Assistant Examiner: Brunsman, David M. Thompson, Hine and Flory LREP CLMN Number of Claims: 15 ECL Exemplary Claim: 1 DRWN No Drawings LN.CNT 378 AΒ The present invention is directed to a stable, rapidly soluble lyophilized injectable composition containing up to about 6% moisture

The present invention is directed to a stable, rapidly soluble lyophilized injectable composition containing up to about 6% moisture and capable of being stored at room temperature comprising the hydrochloric or sulfate salt of a compound selected from the group consisting of (S)-(+)-bis-4,4'-(1-methyl-1,2-ethanediyl)2,6-piperazinedione and (R)-(-)-bis -4,4'-(1-methyl-1,2-ethanediyl)2,6-piperazinedione; wherein said lyophilized composition is prepared from a bulk solution comprising from about 25 mg/mL to about 40 mg/mL of said compound dissolved in a hydrochloric acid or sulfuric acid; wherein the pH of said bulk solution is from about 1.0 to about 2.0. The invention is further directed to an isotonic solution which is formed upon reconstitution of the lyophilizate of the invention with a pharmaceutically acceptable diluent.

=> file caplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	313.09	313.30
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.20	-3.20

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FILE COVERS 1907 - 15 Aug 2008 VOL 149 ISS 8 FILE LAST UPDATED: 14 Aug 2008 (20080814/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s Hofland Kenneth/AU

L13 2 HOFLAND KENNETH/AU

=> dis 113 1-2 bib abs

- L13 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2005:1004605 CAPLUS
- DN 143:279366
- Cancer treatment with topoisomerase II inhibitor, a bis-dioxypiperazine ΤI and radiation
- Hofland, Kenneth; Sehested, Maxwell; Kristjansen, Paul; ΙN Thougaard, Annemette; Jensen, Peter Buhl
- Topotarget A/S, Den. PΑ
- SO PCT Int. Appl., 28 pp. CODEN: PIXXD2
- DT Patent
- English LA

FAN.CNT 1 PATENT NO.				KIND DATE		APPLICATION NO.					DATE								
PI		 ₹0 2005084754 ₹0 2005084754					2005 2006		WO 2005-IB670				20050302						
		W:	AE, CN, GE, LK, NO, SY, BW, AZ, EE, RO,	AG, CO, GH, LR, NZ, TJ, GH, BY, ES, SE,	AL, CR, GM, LS, OM, TM, GM, KG, FI,	AM, CU, HR, LT, PG, TN, KE, KZ, FR, SK,	AT, CZ, HU, LU, PH, TR, MD, GB,	AU, DE, ID, LV, PL, TT, MW, RU, GR, BF,	DK, IL, MA, PT, TZ, MZ, TJ, HU,	DM, IN, MD, RO, UA, NA, TM, IE,	DZ, IS, MG, RU, UG, SD, AT, IS,	EC, JP, MK, SC, US, SL, BE, IT,	EE, KE, MN, SD, UZ, SZ, BG, LT,	EG, KG, MW, SE, VC, TZ, CH, LU,	ES, KP, MX, SG, VN, UG, CY, MC,	FI, KR, MZ, SK, YU, ZM, CZ, NL,	GB, KZ, NA, SL, ZA, ZW, DE, PL,	GD, LC, NI, SM, ZM, AM, DK, PT,	ZW
	MR, NE, SN, AU 2005219034 CA 2557857			•	•			AU 2005-219034 CA 2005-2557857											
	ΕP	EP 1720612							EP 2005-708755					20050302					
		R:	IS,		LI,	LT,		CZ, MC,											
	JP					0927	JP 2007-501380					20050302							
PRAI	GB	2004	070185124 04-4675 05-IB670			А		2007 2004 2005	0302	2					109				

AΒ The present invention relates to a method of treatment of a tumor cell which comprises administering to a subject in need of treatment an effective amount of a topoisomerase-II poison, e.g. etoposide, in

combination with a bis-dioxypiperazine, e.g. dexrazoxane, wherein said subject is further treated with radiation.

- L13 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2000:307970 CAPLUS
- DN 133:187729
- TI Differential cytotoxic pathways of topoisomerase I and II anticancer agents after overexpression of the E2F-1/DP-1 transcription factor complex
- AU Hofland, Kenneth; Petersen, Birgit O.; Falck, Jacob; Helin, Kristian; Jensen, Peter B.; Sehested, Maxwell
- CS Laboratory and Finsen Centres, Rigshospitalet, Copenhagen, DK-2100, Den.
- SO Clinical Cancer Research (2000), 6(4), 1488-1497 CODEN: CCREF4; ISSN: 1078-0432
- PB American Association for Cancer Research
- DT Journal
- LA English
- The transcription factor complex E2F-1/DP-1 regulates the G1-to-S-phase AΒ transition and was associated with sensitivity to the S-phase-specific anticancer agents camptothecin and etoposide, which poison DNA topoisomerase I and II, resp. To investigate the relationship between E2F-1 and drug sensitivity in detail, the authors established human osteosarcoma U-2OS-TA cells expressing full-length E2F-1/DP-1 under the control of a tetracycline-responsive promoter, designated UE1DP-1 cells. Topoisomerase I levels and activity as well as the number of camptothecin-induced DNA single- and double-strand breaks were unchanged in UE1DP-1/tc- cells with > 10-fold E2F-1/DP-1 overexpression. However, UE1DP-1/tc- cells were hypersensitive to camptothecin in both a clonogenic assay and 4 different apoptotic assays. This indicates that camptothecin-induced toxicity in this model is due to the activation of an E2F-1/DP-1-induced post-DNA damage pathway rather than an increase in the number of replication forks caused by the S-phase initiation. In contrast, topoisomerase II α levels (but not topoisomerase II β levels), together with topoisomerase $II\alpha$ promoter activity, increased 2-3-fold in UE1DP-1/tc- cells. Furthermore, the number of etoposide-induced DNA single- and double-strand breaks increased in UE1DP-1/tc- cells together with a rise in clonogenic sensitivity to etoposide, but an equal apoptotic sensitivity to etoposide. The increase in topoisomerase $II\alpha$ promoter activity in UE1DP-1/tc- cells was shown to be due to S-phase initiation per se because it was blocked by ectopic expression of dominant neg. cyclin-dependent kinase 2. In conclusion, overexpression of E2F-1/DP-1 in U-2OS-TA cells is sufficient to increase clonogenic sensitivity to both topoisomerase I- and II-targeted anticancer drugs. However, the mechanism by which this occurs appears to be qual. different. The UE1DP-1 cell model may be used to elucidate post-DNA damage mechanisms of cell death induced by topoisomerase I-directed anticancer agents.
- RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- => s Sehested Maxwell/AU L14 83 SEHESTED MAXWELL/AU
- => s 114 and topoisomerase 13765 TOPOISOMERASE 1840 TOPOISOMERASES 14064 TOPOISOMERASE

(TOPOISOMERASE OR TOPOISOMERASES)

L15 40 L14 AND TOPOISOMERASE

=> s 115 and dioxypiperazine 6 DIOXYPIPERAZINE

=> dis 116 1-2 bib abs

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L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
     2005:1004605 CAPLUS
ΑN
DN
     143:279366
     Cancer treatment with topoisomerase II inhibitor, a bis-
ΤI
     dioxypiperazine and radiation
     Hofland, Kenneth; Sehested, Maxwell; Kristjansen, Paul;
IN
     Thougaard, Annemette; Jensen, Peter Buhl
PA
     Topotarget A/S, Den.
SO
     PCT Int. Appl., 28 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                           KIND DATE
                                                 APPLICATION NO.
                                                                            DATE
                           ____
                                    _____
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                                                 WO 2005-IB670
                            A2
     WO 2005084754
                                     20050915
                                                                            20050302
PΙ
                          A3
                                 20060526
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          CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
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                                                                             20050302
     EP 1720612
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                                    20061115
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                                                                             20050302
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                                     20070927
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                                                  US 2007-591847
                                                                             20070109
                                     20040302
PRAI GB 2004-4675
                            Α
     WO 2005-IB670
                            W
                                     20050302
AB
     The present invention relates to a method of treatment of a tumor cell
     which comprises administering to a subject in need of treatment an
     effective amount of a topoisomerase-II poison, e.g. etoposide, in
     combination with a bis-dioxypiperazine, e.g. dexrazoxane,
     wherein said subject is further treated with radiation.
L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
     1997:556108 CAPLUS
AN
DN
     127:145175
OREF 127:27889a
     Topoisomerase II poison and bis-dioxypiperazine
     derivative combination therapy
     Jensen, Peter Buhl; Sehested, Maxwell
IN
     Jensen, Peter Buhl, Den.; Sehested, Maxwell
PA
SO
     PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
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PATENT NO.
                                    APPLICATION NO. DATE
                  KIND DATE
    WO 9725044 A1 19970717 WO 1997-DK13 19970110
PΤ
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            CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM,
            TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
            IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
            MR, NE, SN, TD, TG
    CA 2242406
                             19970717 CA 1997-2242406
                       A1
    AU 9713677
                        Α
                             19970801 AU 1997-13677
                                                               19970110
    EP 874630
                             19981104
                                        EP 1997-900205
                        Α1
                                                               19970110
    EP 874630
                        В1
                            20030820
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
    AT 247468
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                                        AT 1997-900205
                                                               19970110
    PT 874630
                       T
                             20040130
                                        PT 1997-900205
                                                               19970110
                      T3 20040501
B1 20010724
    ES 2205164
                             20040501
                                        ES 1997-900205
                                                               19970110
    US 6265385
                                        US 1999-101499
                                                               19990308
PRAI DK 1996-22
                       А
                             19960111
                      A
W
    US 1996-603105
                           19970110
                              19960220
    WO 1997-DK13
    The present invention relates to a method for selectively killing tumor or
AΒ
    mammal an effective tumor- or metastasis-killing amount of a
    topoisomerase II poison except doxorubicin, and protecting
    non-tumorous tissue of the mammal against the toxic action of the
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metastatic cells within a defined compartment of the organism of a large mammal, in particular a human, said method comprising administering to a mammal an effective tumor—or metastasis—killing amount of a topoisomerase II poison except doxorubicin, and protecting non—tumorous tissue of the mammal against the toxic action of the topoisomerase II poison by administration of a bis—dioxypiperazine compound In particular, the invention relates to a pharmaceutical kit for selectively killing tumor or metastatic cells within the central nervous system of a large mammal, in particular a human, said kit comprising: a) a dosage unit of a bis—dioxypiperazine and a pharmaceutically acceptable carrier, and b) a dosage unit of topoisomerase II poisons except doxorubicin and a pharmaceutically acceptable carrier.

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=> s Kristjansen Paul/AU
L17 1 KRISTJANSEN PAUL/AU
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=> dis 117 bib abs

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L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
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AN 2005:1004605 CAPLUS

DN 143:279366

TI Cancer treatment with topoisomerase II inhibitor, a bis-dioxypiperazine and radiation

IN Hofland, Kenneth; Sehested, Maxwell; Kristjansen, Paul; Thougaard, Annemette; Jensen, Peter Buhl

PA Topotarget A/S, Den.

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

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                                                                   20070109
                         Α1
PRAI GB 2004-4675
                         Α
                                20040302
     WO 2005-IB670
                         W
                                20050302
AΒ
     The present invention relates to a method of treatment of a tumor cell
     which comprises administering to a subject in need of treatment an
     effective amount of a topoisomerase-II poison, e.g. etoposide, in
     combination with a bis-dioxypiperazine, e.g. dexrazoxane, wherein said
     subject is further treated with radiation.
=> s Thougaard Annemette/AU
            3 THOUGAARD ANNEMETTE/AU
T.18
=> dis 118 1-3 bib abs
L18 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
ΑN
     2007:510771 CAPLUS
DN
     147:268549
     The histone deacetylase inhibitor PXD101 synergizes with 5-fluorouracil to
TΙ
     inhibit colon cancer cell growth in vitro and in vivo
     Tumber, Anthony; Collins, Laura S.; Petersen, Kamille Dumong;
ΑU
     Thougaard, Annemette; Christiansen, Sanne J.; Dejligbjerg,
     Marielle; Jensen, Peter Buhl; Sehested, Maxwell; Ritchie, James W. A.
CS
     TopoTarget UK LTD, Abingdon, OX14 4RY, UK
SO
     Cancer Chemotherapy and Pharmacology (2007), 60(2), 275-283
     CODEN: CCPHDZ; ISSN: 0344-5704
PB
     Springer
DT
     Journal
     English
LA
     Histone deacetylase inhibitors (HDACi) inhibit the growth of cancer cells,
AB
     and combinations of HDACi with established chemotherapeutics can lead to
     synergistic effects. We have investigated effects of PXD101 (HDACi in
     phase II clin. trials) in combination with 5-fluorouracil, on tumor cell
     proliferation and apoptosis both in vitro and in vivo. HCT116 cells were
     studied using proliferation and clonogenic assays. Synergistic inhibition
     of proliferation and clonogenicity was determined by incubation with PXD101 and
     5-fluorouracil, and anal. using CalcuSyn software. The effect of
     combining PXD101 and 5-fluorouracil on apoptosis was examined in vitro using
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PARP-cleavage and TUNEL. Finally, the effectiveness of combining PXD101

clonogenicity was obtained when HCT116 cells were incubated with PXD101

and 5-fluorouracil in vivo was tested using both HT-29 and HCT116 xenograft models. Synergistic inhibition of proliferation and

and 5-fluorouracil. 5-fluorouracil combined with PXD101 also increased DNA fragmentation and PARP cleavage in HCT116 cells. Incubation with PXD101 down regulated thymidylate synthase expression in HCT116 cells. In vivo studies, using mouse HT29 and HCT116 xenograft models, showed improved redns. in tumor volume compared to single compound, when PXD101 and 5-fluorouracil were combined. PXD101 and 5-fluorouracil synergistically combine in their antitumor effects against colon cancer cells in vitro and show enhanced activity when combined in vivo. Based on the results presented herein, a rationale for the use of PXD101 and 5-fluorouracil in combination in the clinic has been demonstrated.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L18 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2006:842431 CAPLUS
- DN 145:284390
- TI Activity of PXD101, a histone deacetylase inhibitor, in preclinical ovarian cancer studies
- AU Qian, Xiaozhong; LaRochelle, William J.; Ara, Gulshan; Wu, Frank; Petersen, Kamille Dumong; Thougaard, Annemette; Sehested, Maxwell; Lichenstein, Henri S.; Jeffers, Michael
- CS CuraGen Corporation, Branford, CT, 06405, USA
- SO Molecular Cancer Therapeutics (2006), 5(8), 2086-2095 CODEN: MCTOCF; ISSN: 1535-7163
- PB American Association for Cancer Research
- DT Journal
- LA English
- AΒ Histone deacetylase inhibitors represent a promising new class of anticancer agents. In the current investigation, we examined the activity of PXD101, a potent histone deacetylase inhibitor, used alone or in combination with clin. relevant chemotherapeutics (docetaxel, paclitaxel, and carboplatin), in preclin. in vitro and in vivo models of ovarian cancer. In vitro activity was examined in ovarian cancer and multidrug-resistant cell lines grown in monolayer culture, and in primary clin. ovarian cancer specimens grown in three-dimensional organoid culture. PXD101 was found to inhibit in vitro cancer cell growth at subto low micromolar IC50 potency, exhibited synergistic activity when used in combination with relevant chemotherapeutics, and effectively inhibited the growth of multidrug-resistant cells. In vivo, PXD101 displayed single-agent antitumor activity on human A2780 ovarian cancer s.c. xenografts which was enhanced via combination therapy with carboplatin. In support of these findings, PXD101 was shown to increase the acetylation of α -tubulin induced by docetaxel and the phosphorylation of H2AX induced by carboplatin. Taken together, these results support the clin. evaluation of PXD101 used alone or in combination therapy for the treatment of ovarian cancer.
- RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L18 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2005:1004605 CAPLUS
- DN 143:279366
- TI Cancer treatment with topoisomerase II inhibitor, a bis-dioxypiperazine and radiation
- IN Hofland, Kenneth; Sehested, Maxwell; Kristjansen, Paul; Thougaard, Annemette; Jensen, Peter Buhl
- PA Topotarget A/S, Den.
- SO PCT Int. Appl., 28 pp. CODEN: PIXXD2
- DT Patent
- LA English

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      A2
      20050915

      WO 2005084754
      A3
      20060526

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PRAI GB 2004-4675
                                20040302
     WO 2005-IB670
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                         W
     The present invention relates to a method of treatment of a tumor cell
AB
     which comprises administering to a subject in need of treatment an
     effective amount of a topoisomerase-II poison, e.g. etoposide, in
     combination with a bis-dioxypiperazine, e.g. dexrazoxane, wherein said
     subject is further treated with radiation.
=> s Jensen Peter Buhl/AU
           43 JENSEN PETER BUHL/AU
L19
=> s 119 and topoisomerase
         13765 TOPOISOMERASE
          1840 TOPOISOMERASES
         14064 TOPOISOMERASE
                 (TOPOISOMERASE OR TOPOISOMERASES)
L20
            23 L19 AND TOPOISOMERASE
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             6 DIOXYPIPERAZINE
             2 L20 AND DIOXYPIPERAZINE
L21
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L21 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
     2005:1004605 CAPLUS
ΑN
DN
     143:279366
ΤI
     Cancer treatment with topoisomerase II inhibitor, a bis-
     dioxypiperazine and radiation
     Hofland, Kenneth; Sehested, Maxwell; Kristjansen, Paul; Thougaard,
IN
     Annemette; Jensen, Peter Buhl
PA
     Topotarget A/S, Den.
SO
    PCT Int. Appl., 28 pp.
    CODEN: PIXXD2
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    Patent
LA
    English
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PRAI GB 2004-4675
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                          W
     The present invention relates to a method of treatment of a tumor cell
AB
     which comprises administering to a subject in need of treatment an
     effective amount of a topoisomerase-II poison, e.g. etoposide, in
     combination with a bis-dioxypiperazine, e.g. dexrazoxane,
     wherein said subject is further treated with radiation.
L21 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
    1997:556108 CAPLUS
ΑN
     127:145175
DN
OREF 127:27889a
     Topoisomerase II poison and bis-dioxypiperazine
     derivative combination therapy
     Jensen, Peter Buhl; Sehested, Maxwell
IN
     Jensen, Peter Buhl, Den.; Sehested, Maxwell
PA
SO
     PCT Int. Appl., 52 pp.
     CODEN: PIXXD2
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    English
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    WO 1997-DK13
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AB The present invention relates to a method for selectively killing tumor or metastatic cells within a defined compartment of the organism of a large mammal, in particular a human, said method comprising administering to a mammal an effective tumor— or metastasis—killing amount of a topoisomerase II poison except doxorubicin, and protecting non—tumorous tissue of the mammal against the toxic action of the topoisomerase II poison by administration of a bis—dioxypiperazine compound In particular, the invention relates to a pharmaceutical kit for selectively killing tumor or metastatic cells within the central nervous system of a large mammal, in particular a human, said kit comprising: a) a dosage unit of a bis—dioxypiperazine and a pharmaceutically acceptable carrier, and b) a dosage unit of topoisomerase II poisons except doxorubicin and a pharmaceutically acceptable carrier.

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1 S KRISTJANSEN PAUL/AU 3 S THOUGAARD ANNEMETTE/AU

L19 43 S JENSEN PETER BUHL/AU L20 23 S L19 AND TOPOISOMERASE

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L18